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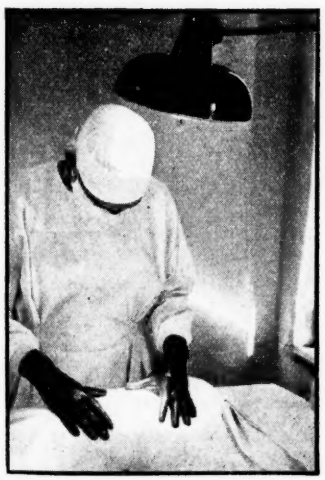

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The Massachusetts Medical Society

The next Annual Meeting of the Massachusetts Medical Society will be held in Worcester, at the Hotel Bancroft, Monday, Tuesday and Wednesday, June 4-5-6, 1934.

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CANCER OF THE PROSTATE AND PROSTATIC DISEASES

BY FREDERICK L. HOFFMAN, LL.D.*

THE general statistics of deaths from cancer of the prostate and prostatic diseases appear to have received quite inadequate consideration. Most of the references are very fragmentary and often derived from more or less untrustworthy sources. Yet it would seem to me that the urgency of such a study or review of the available facts would long since have been called for on account of the apparent increase in the mortality from this type of cancer regardless of the possibility that the increase may be more apparent than real, due to important age changes in the population and improvement in diagnostic procedure. It therefore occurred to me to re-examine the facts of the situation and the results of my preliminary study are presented as follows:

By way of introduction I quote a recent statement on "The Prostate and Seminal Vesicles from the Treatise on Human Cancer" by Dr. Arthur P. Stout, Associate Professor of Surgery, Columbia University, published in Philadelphia 1932.

> "Cancer of the prostate gland, although it is the commonest site for cancer among the male genital organs, according to von Berencsy and von Wolff (1924), is one of the less frequent causes of death from cancer in general. In the group studied by us there was an hospital incidence of 1.83 per cent (34 cases among 1862 cancers seen in ten years). It is remarkable because it is a disease of old age; the average age at onset lies between sixty and seventy years (it was sixty-five years in our group); because it is rarely cured and because it is very often preceded by hypertrophy of the prostate. Since hypertrophy of the prostate is generally accompanied by epithelial hyperplasia and is probably due to some irritational processes associated with involution, the cycle which we believe is associated with the initiation of all cancers is suggested here. As in all other parts of the body, chronic irritation and epithelial hyperplasia are followed by cancer formation only in a relatively small number of instances. Renaud (1925) has shown that the death-rate for cancer of the prostate is increasing; a phenomenon which may be explained on the basis that this is distinctly a disease of old men and that the proportionate number of old men to the general population has been steadily increasing. Prostate cancers are also remarkable because of the frequence with which they metastasize and especially because of the frequence with which the metastases lodge in bones. Bone metastases are observed in about 25 per cent of clinical cases and have been reported in as high as 70 per cent of autopsies."

I cannot agree that the situation regarding cancer of the prostate is one of less importance than that of many other forms of cancer receiving much more extended consideration. Using the data for 1929 for the United States registration area, I give the following comparative statistics: deaths from cancer of the rectum, 5,018, prostate 4,359, bladder 3,586, buccal cavity 3,538, skin 2,904, pancreas 2,802, lungs and pleura 2,304. The foregoing comparison may well arrest attention as visualizing with approximate accuracy the relative position of cancer of the prostate among kindred groups of malignant affections, nearly all of which apparently are receiving much more consideration on the part of research workers and the profession generally.

I give first a table showing deaths from cancer of the prostate in the United States registration area as compiled by the Census Office 1920-1931, representing 38,486 deaths. In this table I also give the rates per 100,000 of male population.

MORTALITY FROM CANCER OF THE PROSTATE, U. S. REG. AREA, 1920-1931

Rate per 100,000 of Male Population

	Deaths	Rate		Deaths	Rate		Deaths	Rate
1920	1,597	3.6	1924	2,558	5.0	1928	4,145	7.3
1921	1,672	3.6	1925	3,068	5.9	1929	4,359	7.5
1922	2,022	4.2	1926	3,427	6.4	1930	4,648	7.7
1923	2,282	4.6	1927	3,784	6.8	1931	4,924	8.0

As shown by the preceding table deaths from cancer of the prostate have increased from a rate of 3.6 per 100,000 male population in 1920 to 8.0 in 1931. In other words the death rate has more than doubled during the intervening period of years. How far this is the result of age changes and improved methods of diagnosis and treatment, of course, is a debatable question. But as regards the age question, I am of the opinion that the effect has been of small importance during the period under review. As to diagnostic procedure and treatment considerable progress has been made and that of course may have been effective in raising the number of deaths to a measurable degree. At the same time it seems to me that it goes without saying

*Hoffman, Frederick L.—Consulting Statistician, Prudential Insurance Co. For record and address of author see "This Week's Issue," page 556.

that there has been an actual increase in deaths from cancer of the prostate which cannot be explained away.

I give next a table of deaths from cancer of the prostate in England and Wales for the period 1921-1930, later statistics not yet being available. In this table I have also included deaths and rates for Scotland for the same period of years.

MORTALITY FROM CANCER OF THE PROSTATE—1921-1930

Rate per 100,000 Male Population

	England and Wales		Scotland	
	Deaths	Rate	Deaths	Rate
1921	756	4.18	70	2.98
1922	840	4.62	70	2.98
1923	975	5.33	101	4.31
1924	1,022	5.55	121	5.17
1925	1,116	6.03	136	5.81
1926	1,145	6.15	119	5.09
1927	1,172	6.26	115	4.93
1928	1,353	7.18	165	7.07
1929	1,430	7.55	149	6.39
1930	1,434	7.53	174	7.47

The two tables may be summarized in the statement that at the present time the death rate from cancer of the prostate is 8.0 per 100,000 male population for the United States Registration Area and 7.5 for England and Wales and 7.5 for Scotland, a remarkable conformity to practically an identical experience. I regret that I cannot give corresponding rates for other countries at this time but I have the matter under consideration and will communicate important data later.

Deaths from cancer of the prostate are not given according to age for this country, but I have compiled the data for England and Wales for the period 1921-1930 showing the actual deaths for the two five-year periods and the percentage distribution for each period likewise.

MORTALITY FROM CANCER OF THE PROSTATE IN ENGLAND AND WALES—1921-1930

	1921-1925		1926-1930	
Age	Deaths	Per Cent	Deaths	Per Cent
Under 35	12	0.25	10	0.15
35-39	8	0.17	13	0.20
40-44	20	0.42	17	0.26
45-49	66	1.40	60	0.91
50-54	181	3.84	210	3.21
55-59	386	8.20	459	7.02
60-64	714	15.16	990	15.15
65-69	1,044	22.17	1,400	21.43
70-74	1,063	22.57	1,595	24.41
75-79	785	16.67	1,124	17.20
80-84	314	6.67	472	7.22
85 and over	116	2.46	184	2.82
Total	4,709	100.00	6,534	100.00

It is shown by this table that cancer of the prostate may appear as early as at ages under 35, there having been 22 deaths during the ten years under review. At ages 35-39 there were 21 deaths, at 40-44, 37; and at 45-49, 126. After this the deaths rapidly increase until a maximum figure is reached at the age period 70-74. This table sustains the conclusion that the age change in the population has not been of sufficient significance to explain the actual increase from 4,709 deaths during the five years 1921-1925 to 6,534 in 1926-1930.

To eliminate the age factor entirely I add some statistics of cancer mortality for certain organs and parts on a standardized basis for England and Wales for years 1901-1930. I have selected for the present purpose, cancer of the tongue, esophagus, liver, lung, pancreas and bladder.

CANCER MORTALITY, ENGLAND AND WALES, 1901-1930

Rate per 100,000

	Tongue	Esophagus	Liver	Lung	Pancreas	Prostate
1901-1910	4.31	5.12	—	1.02	1.45	11.8
1911-1920	5.08	6.06	8.71	1.27	1.67	26.5
1921-1930	4.61	6.42	6.10	2.52	2.63	47.7

This is an exceedingly instructive comparison clearly showing the numerical importance, as well as the relative importance, of cancer of the prostate and kindred cancer affections.

According to a tabulation of cancer of the prostate ascertained in connection with my San Francisco Cancer Survey, based on 683 deaths in different localities of the United States and Canada, I find that the average age at death was 68.2 years, the lowest average age being reported for the New Orleans colored population, or 58.2 years, but the number of deaths is very small. So far as it is possible to judge, cancer of the prostate is much less common among the colored population than among the white but that of course may be due to failure of diagnosis.

For the purpose of comparison I give the average age at death for kindred cancer affections, having reference, of course, to the male population only. Cancer of the buccal cavity 60.6 years; esophagus 62.4; skin 63.7; rectum 60.8; tongue 59.6; prostate 68.2; bladder 64.2; larynx 60.4; lung 53.0 and pancreas 59.3.

I am also able to give some information concerning the known duration of the disease for cancer of the prostate ascertained in connection with my San Francisco Cancer Survey for a number of localities throughout this country and Canada. For all forms of cancer the average known duration of the disease was 15.4 months; for cancer of the prostate 19.7 months; tongue 14.7 months; esophagus 10.4 months; rectum 17.6 months, bladder 18.9 months, larynx 14.3 months; lung 11.0 months and pancreas 9.5 months. For the time being I am only giving the facts as I have found them without reflecting on their relative importance.

A discussion of cancer of the prostate cannot very well ignore some observations on deaths from diseases of the prostate. These may or may not have been potentially precancerous or

actually so without the facts being ascertained at autopsy, or by means of competent pathological examination. In the table below I give the deaths from diseases of the prostate in the United States Registration Area and the rates per 100,000 of male population.

MORTALITY FROM DISEASES OF THE PROSTATE, U. S. REG. AREA, 1920-1931
Rate per 100,000 Male Population

	Deaths	Rate		Deaths	Rate		Deaths	Rate
1920	3,669	8.2	1924	4,842	9.5	1928	6,264	11.0
1921	3,804	8.2	1925	5,200	9.9	1929	6,407	11.0
1922	4,117	8.6	1926	5,600	10.4	1930	6,464	10.8
1923	4,540	9.2	1927	5,761	10.4	1931	6,541	10.6

According to this tabulation the death rate from diseases of the prostate in the United States registration area has increased from 8.2 per 100,000 male population in 1920 to 11.0 during 1928 and 1929, decreasing to a rate of 10.6 in 1931. It is thus shown that while both cancer of the prostate and diseases of the prostate have increased during recent years the latter affection is relatively more common than the former.

I give the corresponding figures for England and Wales 1921-1931 showing an increase in the rate of frequency from 11.8 per 100,000 in 1921 to 21.1 in 1931. The English rate therefore is just about double the American rate, a fact to which I have never seen any attention called before. In other words while cancer of the prostate prevails to about the same extent in this country and in England and Wales, diseases of the prostate are twice as common in the latter country as in the former.

MORTALITY FROM DISEASES OF THE PROSTATE, ENGLAND AND WALES, 1921-1931
Rate per 100,000 Male Population

	Deaths	Rate		Deaths	Rate		Deaths	Rate
1921	2,124	11.8	1925	2,665	14.3	1929	3,760	19.8
1922	2,121	11.6	1926	2,705	14.5	1930	3,803	19.9
1923	2,288	12.5	1927	3,172	16.9	1931	4,039	21.1
1924	2,479	13.4	1928	3,407	18.0			

Without reflecting in detail upon the foregoing statistics I feel that they should make a useful contribution toward a better understanding of the numerical aspects of the cancer problem. However, to make this comparison as complete as possible I may add the statement that in Scotland in 1931 there were 157 deaths from cancer of the prostate compared with 364 deaths from diseases of the prostate. Deaths from diseases of the prostate in Scotland have increased from 256 in 1921 to 364 in 1931. In Holland there was an extraordinary increase from 318 deaths from diseases of the prostate in 1924 to 600 in 1929. The rate shows a persistent increase in Holland from 1911 onwards, the change having been as follows: 1911-1915 6.6 per 100,000; 1916-1920 8.2; 1921-1923 8.6; 1924-1928, 12.2; 1929, 15.5. In Australia the rate increased from 8.2 per 100,000 male population in 1919 to a maximum of 12.0 in 1927, while the actual deaths increased from 234 in 1918 to 319 in 1923; 380 in 1927; 394 in 1929; 418 in 1930 and 446 in 1931. In the Dominion of Canada in 1932 the number of deaths from cancer of the prostate was 377 while the number of deaths from diseases of the prostate during the same year was 878. Deaths from disease of the prostate in Canada increased from 638 in 1927 to 878 in 1932.

Thus the increase in diseases of the prostate seems to be world wide and well deserving of international studies comprehending all the principal countries. Unfortunately at the present time I am unable to contribute much additional information to this interesting situation.

Before concluding this discussion it seems appropriate to add a few observations upon recent contributions to the study of carcinoma of the prostate. Among the earlier papers is that of H. C. Bumpus, contributed to *Surgery, Gynecology and Obstetrics*, 1926, mentioned as being A Clinical Study of 1000 Cases of an average of 65 years. The average duration of the disease from the first symptom to death in 485 cases with no treatment was 31 months. With metastases two-thirds of the patients died under nine months from the time of examination. When no metastases were found after careful examination, the average duration of life was 1 year, although isolated cases lived considerably longer, e.g., four lived over three years, and two over ten. In 243 cases metastatic spread was demonstrable. In 44 per cent it had affected the lymphatics. As a result of completed records of 164 cases, the author concluded that surgery was unsatisfactory when the disease had advanced sufficiently to be positively diagnosed.

In the Ewing Memorial Volume, New York, 1931, is an important contribution on Carcinoma of the Prostate by Dr. Benjamin S. Barringer of New York who introduces his subject with the statement that:

> "Carcinoma of the prostate still holds its place as the most baffling of urological conditions. We know little of its etiology. In but a small percentage of cases is the diagnosis made sufficiently early to give any sort of treatment a fair chance of success. Even if an early diagnosis be made there is no general agreement as to the best way to treat this neoplasm. We hold that the possibilities of radical surgery have been thoroughly exploited while the effective use of radiation is still far from the practical limits of its application to this disease."

In a series of 280 cases the earliest age period was under 34 with one patient, and the oldest 85 to 89, also with one patient. Most of the cases occurred at ages 50 to 79.

Among the initial symptoms in the 280 cases are frequency of micturition occurring in 47.8 per cent of the cases, difficulty in 34.2 per cent, nocturia in 28.8 per cent, dysuria in 21.4 per

cent, retention in 16.7 per cent. Constipation was met with in only 3.5 per cent of the cases and loss of weight in 2.8 per cent.

Among the secondary symptoms occurring in the 280 cases are nocturia in 18.2 per cent, retention in 16.0 per cent, hematuria in 13.9 per cent, frequency in 12.1 per cent, dysuria in 11.4 per cent. Constipation was recorded in 4.6 per cent. The conclusions are summarized as follows:

> "There is no general agreement among urologists as to the best therapy for carcinoma of the prostate.
>
> It is held that the possibilities of radical surgery are exhausted, certain features in the natural history of the disease precluding the effective application of this form of treatment.
>
> It is shown that there has been gradual improvement in the control of carcinoma of the prostate by radiation.
>
> The age incidence and symptoms displayed in a series of 280 cases of carcinoma of the prostate are tabulated.
>
> The early diagnosis of the disease is discussed and the use of a new biopsy technic is suggested.
>
> Treatment by radiation is discussed. Higher tissue doses and cystotomy are believed essential to the more effective control of prostatic carcinoma."

In the July issue of the *American Journal of Cancer Research*, 1932, is an important paper on Cancer of the Prostate by Dr. Russell S. Ferguson of Memorial Hospital, New York City. It contains a tabulation of the incidence of early and borderline cancers in supposedly benign prostatic disease as follows:

INCIDENCE OF EARLY AND BORDERLINE CANCERS IN SUPPOSEDLY BENIGN PROSTATIC DISEASE

Authors	Prostates Examined	Early or Borderline Cancer Found
Wilson and McGrath	468	73 early
Swan	28	4 early
Eastes and Fletcher	678	58 borderline and early
Wade	134	14 early
Thomson Walker	100	16 early
Bugbee	7	7 early
Hirsch and Schmidt	11	11 early
Randall	312	17 early and advanced
Total	1,738	200

This table is amplified by a clinical index of malignancy as follows:

CLINICAL INDEX OF MALIGNANCY

Index Factors	Group A (Least Malignant)	Group B (Intermediate)	Group C (Most Malignant)
Age	Over 65	55 to 65	Under 55
Residual urine	200 cc. and over: frequent complete retention	100 to 200 cc.	Under 100 cc.
Duration of symptoms	Over 20 months	10 to 20 months	Under 10 months
Extent of disease	No pain, no demonstrable metastases	Pain, no demonstrable metastases	Pain and demonstrable metastases
Prognosis untreated	30 months to many years	7 to 30 months (average 18 months)	Up to 1 year (average 6 months)
Percentage of 501 cases	62 per cent	26 per cent	12 per cent

The conclusions are summarized below:

> "It is shown that cancer may and does arise in any portion of the prostate or its accessory lobules.
>
> "Three clinical types of carcinoma of the prostate are described. Each is characterized by its own clinical syndrome, pathological features, and prognosis.
>
> "Pain, other than that due to urinary obstruction or bony metastasis, is held to be pathognomonic of lymphatic extension, especially in the peri-neural lymphatics.
>
> "It is urged that the end results of treatment be evaluated on the basis of the clinical classification of the disease.
>
> "The value of aspiration biopsy in the determination of radiosensitivity is stressed.
>
> "The selection of therapy is discussed.
>
> "The effects of irradiation upon the tissues of the tumor and adjacent structures are enumerated.
>
> "An original technic of interstitial radiation, providing greater accuracy in the placement of gold seeds, is described."

A more recent discussion is that by Drs. John R. Caulk and S. B. Boon-Itt on Carcinoma of the Prostate in the *American Journal of Cancer Research* of September, 1932. These authors introduce their subject with the statement that "One of the most vital problems confronting the urological surgeon today concerns the early recognition and treatment of cancer of the prostate." Mention is made of the fact that "The first case of carcinoma of the prostate was recognized by Langstaff in 1817. Billroth in 1867 first attempted to treat this condition by surgery. The frequency of the neoplasm was not well recognized until 1900, when Albarran and Halle intimated that it was not uncommon. Since then a number of studies have been made on the subject, various facts have been brought to light, and many helpful suggestions presented by different investigators." The authors state that "In spite of the numerous studies already made, the management of carcinoma of the prostate is still far from satisfactory." They quote various statistics of incidence, more or less contradictory, concluding that "the toll is far from insignificant." They give the following table of microscopic diagnosis of tissue removed from prostates, limited to 107 cases.

MICROSCOPIC DIAGNOSIS OF TISSUE REMOVED FROM PROSTATE (107 CASES)

	Positive	Negative
Tissue removed by Caulk's cautery punch (64 cases)	52 cases (81.4%)	12 cases
Tissue removed by prostatectomy (43 cases)	42 cases (97.6%)	1 case
Total	94 cases	13 cases

They mention an instance of cancer of the prostate in a youth seventeen years of age. The mean average age of 194 cases was 63.4 years, the youngest case in the series being 25 and the oldest, 85 years.

Concerning symptoms, the chief complaints were referable to the urinary system in 142 of the 194 cases, or 73.7 per cent with a mean average duration of three years. The chief complaints are given in tabular form as follows:

CHIEF COMPLAINTS AS GIVEN BY PATIENTS WHEN FIRST SEEN, WITH AVERAGE DURATION OF COMPLAINT

	Number of Cases	Average Duration of Complaint
Complaints Referable to Urinary System, 143 Cases (73.7%)		
Obstruction to urination (ranging from slight difficulty to retention)	61 (42.6%)	3 years 2 mos.
Frequency of urination	51 (35.6%)	2 " 11 "
"Bladder trouble"	16 (11.2%)	3 " 8 "
Painful urination	7 (4.9%)	3 " 1 mo.
Nocturia	6 (4.3%)	1 year 10 mos.
Hematuria	1	
Dribbling	1	
Total	143 cases	3 years (Average)
Complaints Suggestive of Extension or Metastasis, 42 Cases (21.6%)		
Pain in lower back	14 cases	
Pain in legs	10	
Weakness and loss of weight	8	
Pain in rectum	4	
Gastrointestinal symptoms	4	
Edema of lower extremities	2	
Total	42 cases	
Silent Cases	9 (4.64%)	

The discussion is exceedingly interesting but hardly admits of convenient abbreviation. It includes a discussion of first symptoms as noted in 194 cases, general symptoms, blood picture, blood pressure readings, as to which I give the following tabulation showing the relation of blood pressure to urinary disturbances in 125 cases:

RELATION OF BLOOD PRESSURE TO URINARY DISTURBANCES IN 125 CASES

	Total Cases	Blood Pressure Reading Within Normal Variation	Blood Pressure Reading Higher Than Normal Variation	Blood Pressure Reading Lower Than Normal Variation
All cases regardless of complaints	125	67 cases (53.6%)	33 cases (26.4%)	25 cases (20.0%)
Cases with urinary symptoms as chief complaints	90	49 cases (54.4%)	30 cases (33.3%)	11 cases (12.3%)
Cases with non-protein nitrogen higher than 50 mgm. per 100 cc. of blood	21	12 cases (57.1%)	7 cases (33.3%)	2 cases (9.6%)

The authors next discuss the size of the prostate and cystoscopic findings in 105 cases, followed by a study of metastases and necropsy findings in 17 cases. All of this must be consulted in the original since it is not possible to abbreviate it to advantage. They also discuss the question of treatment at considerable length, making this paper one of the most important on the subject ever published. I give the summary of conclusions below. The paper is amplified by an extended bibliography which is very useful.

"The frequency of prostatic cancer warrants attention and demands early recognition. Chronic inflammation of the prostate may be a predisposing cause. The cautery punch operation in conjunction with radium and x-ray therapy appears to be the method of choice for relieving obstruction and retarding the progress of the disease. Seventy-two per cent of the cases thus treated received complete relief of obstruction. Twenty-nine per cent of the patients lived or are living over three years, 10 per cent over five years, a longer duration of life than that afforded by prostatectomy. The mortality from the operation, in spite of the fact that it was done in many instances upon extremely ill patients, upon whom prostatectomy would not have been considered, is 2.5 per cent. The mortality rate from prostatec-

tomy in this disease in our clinic is 17 per cent. Hospitalization has been less than with prostatectomy. The punch operation affords a definite means of accurately diagnosing cancer of the prostate in 80 per cent of all cases, early or late, which indicates that the disease, even in apparently early cases, is present throughout the substance of the gland."

American Society for the Control of Cancer, Chicago, October 7, 1933.

PEPTIC ULCER: ITS SURGICAL MANAGEMENT*

BY JAMES C. MC CANN, M.D.†

INTRODUCTION

THE rôle of surgery in the management of peptic ulcer should be that of a special therapeutic measure used to cope with complications, or to control those ulcers which fail to respond to medical treatment. Brown[1], at the Sippy Clinic, estimates that twenty per cent of ulcers treated in a medical unit will require surgical treatment. Nielson[2] concludes from a statistical analysis of a large series of cases treated medically, that whereas sixty per cent of cases with a history of only six months' duration will respond to medical treatment, only five per cent with a history of ten years' duration will so respond. When the period of active symptoms ranged between these time limits, the response to medical treatment varied inversely as the duration of the symptoms. Our experience is that with a large proportion of referred surgical work, operation will be advisable in thirty to fifty per cent of the cases. Many factors such as the age of the ulcer, the extent of the pathology, the complications, the economic status and coöperative capacity of the patient, will determine the number of lesions requiring surgical treatment.

The operative technique for treatment of ulcer of the stomach and duodenum is after fifty years of progress, highly developed and standardized. That point is now reached where a surgeon must individualize each ulcer as viewed at the operating table, and select the operation best suited to each particular lesion. This selection will be done accordingly as one adheres to the precepts of the school which recommends conservative or radical surgery for ulcer. The selection must be made quickly, with a soundness of surgical judgment which equals in importance the accuracy and facility with which the operation itself is done. Adhering to the school of conservative surgery, we found a review of 105 consecutive cases operated upon during the period between January, 1930 and September, 1932 by Drs. M. F. Fallon, John Fallon and the author, to be instructive. The series includes a comprehensive list of operative procedures which meet satisfactorily most of the exigencies which arise in the surgical management of ulcers. It emphasizes the need of complete familiarity with this field, if a surgeon is to do full justice to patients who submit themselves for operation upon this vital organ.

The factors which condition the selection of the type of operation best suited for a particular ulcer are two, namely, the extent of the lesion, and its location. The larger, more indurated and calloused is the ulcer, and the farther its location shifts from the duodenum across the pylorus into the stomach, the more extensive will be the operation required. Our series, though small, bears out this generalization, and emphasizes the need for full mastery of all technical methods used in this field, if all situations are to be met adequately.

DUODENAL ULCER

I. *Pyloroplasty*

- A. Partial Duodenectomy. (Fig. IA)
- B. Partial Duodenectomy and Cauterization (Fig. IB)

A. Partial duodenectomy is the most conservative operation for ulcer, and is applicable only to simple ulcers. Two factors condition its use; first, the lesion must be small, in the first half inch of the anterior wall of the duodenum, and free of all extensive adhesions and deforming cicatrices; secondly, the first portion of the duodenum must be sufficiently long, mobile, and wide to permit free delivery from the abdomen. A fore-shortened duodenum retracted by a calloused ulcer against the spine, is not suited to this procedure. Brief technical descriptions of each type of operation will be given.

Technique (Fig. IA): The stomach is delivered and retracted to the left. The pyloric vein is ligated at the greater and lesser curvatures. Through a small longitudinal incision in the middle of the anterior wall of the stomach one inch proximal to the pylorus, the stomach contents are aspirated. Beginning at this incision, a rectangular piece of gastric and duodenal wall, including the ulcer, is excised. Two lines of excision extend from the first incision toward the greater and lesser curvatures at the pylorus thus removing half the sphincter. From the pylorus the lines of excision converge to a point in the middle of the first portion of the duodenum beyond the ulcer. This excised tissue contains the ulcer and the anterior third of the sphincter. The edge of the gastric mucosa is sutured to the edge of the duodenal mucosa in a longitudinal direction. This layer is infolded

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by a second seromuscular suture line. This line is reinforced by omental tabs.

B. Partial duodenectomy and cauterization are used when an anterior wall ulcer suitable for pyloroplasty is associated with a posterior wall, or "kissing ulcer". The latter ulcer, usually exposed after the anterior wall ulcer has been excised, is typically a crater type, located just beyond the pylorus.

Technique (Fig. IB): The anterior wall ulcer is excised in the manner described above. The posterior wall ulcer is well exposed and the surrounding duodenal wall protected by moist packs. The lesion is cauterized until the base is destroyed and the mucosal edges around the ulcer are freed. The free mucosal edges are then approximated over the crater defect by deep interrupted catgut sutures. The plastic repair is then carried out in the manner described.

Discussion: Pyloroplasty was first performed by Heinecke in 1886 and independently by Mikulicz in 1887. It consisted originally of a longitudinal incision through the pylorus, which was resutured in a vertical direction, thus increasing the width of the opening at the pylorus. Since then many forms of plastic operations have been devised. Finney published his original method in 1902. Since then other methods have been developed by Horsley, Balfour, and Judd, and have been widely used. Balfour suggested the cautery destruction of ulcers in 1914.

We used pyloroplasty in eight cases of our series. Judd[3] thinks that it may be applied to fifty per cent of ulcers. Two of our series had associated posterior wall ulcers which were destroyed by cautery. The merit of pyloroplasty is that it removes the ulcer, but retains the normal continuity of the gastro-intestinal tract. The operation described above removes half the pyloric sphincter and cripples the muscular action of the distal portion of the antrum. This factor and the widened lumen overcome spasm and the retention of acid, and permit more rapid emptying of the stomach. It may also reduce the acidity of the gastric juice by permitting a freer regurgitation of alkaline duodenal juices into the stomach. Satisfactory results are obtained in eighty per cent of operations, with some relief in the others. In the few cases in which ulcers recur, the whole field of more radical surgery is still available.

DUODENAL ULCER 91 OPERATIONS.

TYPE OF OPERATION	NO.	TYPE ULCER	TECHNICAL FACTORS	DIAGRAM.
I PYLOROPLASTY A. PARTIAL DUODENECTOMY	5	SMALL ANT. WALL ULCER ½ OF PYLORUS	MOBILE DUODENUM NO CICATRICES	I
B. SAME AND CAUTERIZATION	3	POSTERIOR WALL KISSING ULCER		
II GASTRO-ENTEROSTOMY A. POSTERIOR 1. VERTICAL 2. TRANSVERSE ANTI-PERISTALTIC 3. ISOPERISTALTIC	59 8 4	CICATRIX DEFORMITY CRATER		II
B. ANTERIOR WITH ENTERO-ENTEROSTOMY	3	SAME		
III CLOSURE PERFORATION A. SIMPLE CLOSURE	4	CICATRIX DEFORMITY PERFORATED	OVER 6 HOURS POOR RISK	III
B. CLOSURE AND GASTRO ENTEROSTOMY	3	SAME	UNDER 6 HOURS GOOD RISK STENOSIS PYLORUS	
IV DEVINE EXCLUSION	2	CICATRIX DEFORMITY PENETRATION HEMORRHAGE	POOR PROTECTION FROM G.E. OPEN PYLORUS POOR RISK FOR RESECTION	IV

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II. *Gastro-Enterostomy*

A. Posterior
1. Vertical (Fig. IIA_1).
2. Transverse { Antiperistaltic (Fig. IIA_2). / Isoperistaltic (Fig. IIA_3).

B. Anterior with Entero-enterostomy (Fig. IIB.)

A. Posterior gastro-enterostomy, the next least radical operation to pyloroplasty, is used

when exploration reveals an extensive cicatrized ulcer of the duodenum which foreshortens, contracts, or obstructs the duodenum. A direct attack upon such extensive pathology by a plastic operation would not be feasible. An indirect drainage operation to induce healing of the ulcer is offered by gastro-enterostomy. The anastomosis of the jejunum to the stomach may vary in three particulars; first, in whether the anastomosis is placed on the anterior or posterior wall of the stomach; secondly, in the direction in which the jejunum is apposed to the stomach wall, vertically or transversely; thirdly, in whether the loop of anastomosed bowel (transverse), passes in the direction of gastric peristalsis (isoperistaltic), or in the reverse direction (antiperistaltic). The posterior vertical type of anastomosis we used whenever possible.

Technique (Fig. IIA$_1$, A$_2$, A$_3$): For a posterior type, the stomach, transverse colon and omentum are delivered and rotated on a transverse axis. A fold of the posterior wall of the stomach is delivered through a rent in the mesocolon. The dependent point of the posterior wall is grasped with an Allis forceps. The posterior wall is delivered further by traction on the forceps, and by freeing adhesions from the pancreas, until the lesser curvature is freely delivered. Here a second Allis forceps is placed a half inch nearer the pylorus than the Allis at the greater curvature. These two markers establish an approximately vertical line in the mid-portion of the posterior wall of the stomach. The edges of the mesocolic rent are sutured high on the posterior wall of the stomach on each side of the fold in the Allis clamps. The fold is then caught in a rubber-covered clamp. The jejunum is accurately identified where it emerges from under the mesocolon, and a loop of it caught in a rubber-covered clamp as close to the point of emergence as may be done without tension. The clamp is approximated to that on the posterior wall of the stomach. The apposed serous surfaces are united by a seromuscular continuous catgut suture for a distance of three inches. The serosa and muscularis of the stomach are incised for a little less than three inches, parallel to the suture line and a quarter of an inch away from it. The vessels in the submucosa are doubly clamped. The mucosa and submucosa are incised in a line between these clamps, and the vessels tied. All layers of the jejunum are cut through by a similar incision. The adjacent inner edges of the openings in the stomach and jejunum are united by a continuous catgut suture through all coats. This suture is continued along the outer mucosal edges, thus establishing the anastomotic stoma. The clamps are removed and the seromuscular suture line is resumed and carried anteriorly, infolding the mucosal suture line. In the transverse type of anastomosis the two Allis forceps are placed at the ends of a four-inch fold close to and parallel with the greater curvature, and as close to the pylorus as possible. This fold is caught in a rubber-covered clamp. A loop of jejunum is caught in a clamp passing in the direction of gastric peristalsis (isoperistaltic), or in the reverse direction (antiperistaltic), and the two approximated. The anastomosis is then made in the manner described.

Anterior gastro-enterostomy with entero-enterostomy is used for the same type of lesion as above, when technical factors make a posterior anastomosis inadvisable. Such factors are a narrow costal arch with a high lying stomach, extreme deposits of fat in the mesocolon, or foreshortening of the mesocolon. We encountered one contracted mesocolon, shortened to an inch by adhesions from an attack of peritonitis in early life. Reformation of adhesions would have endangered the stoma of a posterior gastro-enterostomy. The patient was not a satisfactory risk for resection because of recent severe hemorrhage, so an anterior gastro-enterostomy was done.

Technique (Fig. IIB): The jejunum is identified and carried up over the colon and omentum to the anterior surface of the stomach. The loop is alternately shortened and lengthened, and approximated to the stomach at a point where it swings without tension around the transverse colon and omentum. This is usually about eighteen inches beyond the duodenojejunal flexure. A segment is caught in a rubber-covered clamp and apposed to a line on the anterior wall of the stomach three or four inches proximal from the pylorus and near the greater curvature. An anastomosis to the stomach is made as described under posterior gastro-enterostomy. After it is completed the afferent loop is attached to the stomach above and proximal to the anastomosis by a few interrupted sutures so as to prevent kinking. This must be supplemented by an entero-enterostomy between the afferent and efferent loops of the jejunum, so as to drain the secretions from the proximal loop, and prevent its dilatation by secretions. A point is selected in the proximal loop distal to where it turns upwards around the colon and omentum, and three inches of it are caught in a rubber-covered clamp. A corresponding point on the descending loop is similarly placed in a clamp, and the two are approximated. A posterior seromuscular suture is placed between the two loops. Both loops are opened by incisions parallel to the line of anastomosis. The inner mucosal edges are sutured together by a continuous through and through suture, which is continued anteriorly thus establishing the stoma. The seromuscular layer is then continued anteriorly infolding the mucosal suture line.

Discussion: Gastro-enterostomy was first performed by Wölfler (1881) at the suggestion of his assistant Nicoladoni. It was a long loop anterior type, done for cancer of the pylorus, and postdated by two years Péan's attempt at pylorectomy (1879). Braun many years later (1892) suggested an entero-entero-anastomosis between the afferent and efferent loops of the long loop anterior anastomosis. Courvoisier first performed a posterior (retro-colic) gastro-enterostomy in 1882, but the patient succumbed on the thirteenth day from peritonitis. In 1885 v. Hacker improved on this method of posterior gastro-enterostomy by carefully identifying the proximal jejunum where it emerges from under the mesocolon, and by suturing the rent in the mesocolon to the posterior wall of the stomach. Peterson first suggested a short loop posterior gastro-enterostomy, and it was first used by his

chief Czerny in 1901. Gastro-enterostomy was used originally only for obstructing carcinoma. Doyen in 1898, first used it for duodenal ulcer.

In our series gastro-enterostomy was done in eighty-one instances. Only three of these were anterior types of anastomoses. Of the seventy-eight posterior anastomoses, sixty-eight were of the vertical type; seven were transverse antiperistaltic types, and three were transverse isoperistaltic types. The posterior type of anastomosis is preferable because it can be most quickly done, and because it has the lowest incidence of gastro-jejunal ulcers. A transverse type of anastomosis was used when a high lying small stomach, obesity, or extensive adhesion of the posterior wall of the stomach to the pancreas, made free delivery of the stomach for a vertical type of anastomosis too difficult. The antiperistaltic direction was preferred in transverse anastomoses as the loop hung more satisfactorily in this position. Occasionally the isoperistaltic direction gave a more freely hanging loop when the jejunum passed from under the mesocolon far over to the left of the midline, or when it had a short immobile mesentery.

Gastro-enterostomy is an indirect operation intended to aid the healing of an irremovable ulcer, and to protect its host from the complications of a progressing chronic ulcer. This is accomplished by mechanical and chemical means. Mechanically, it drains part of the chyme and coarse irritating food from the stomach, through the new stoma into the jejunum, thus shortening the emptying time. This relieves the ulcerated duodenum from exposure to the whole meal during the entire period of normal emptying. When the period of normal digestion is completed, the relaxed stomach permits the final free acid aliquot to drain directly through the stoma into the jejunum, thus sparing the ulcer from the action of free hydrochloric acid. Chemically, the alkaline duodenal juices which are drained back into the stomach lower somewhat the concentration of the acidity of the juice.

The result of gastro-enterostomy for definite chronic ulcers, has proved highly satisfactory in American clinics. There is a marked uniformity in the reports of eighty to ninety per cent satisfactory results from all but a few clinics. Jejunal ulcers are reported at from two to five per cent in most clinics, quite at variance with the figure thirty-three per cent reported from Mt. Sinai in New York, and from the Continent. The rôle of this operation is not only cure, but also protection from complications. Perforation, which occurs in possibly five per cent of chronic ulcers, is extremely rare after gastro-enterostomy; hemorrhage is reduced from an incidence of fifteen to twenty-five per cent with a mortality of three to five per cent, to an incidence of about nine per cent with a negligible mortality; recurrent symptoms which are difficult to control before operation, are easily controlled by moderate dietetic care after operation. In the two to five per cent of recurrent ulcers, the whole field of more radical surgery is still available.

III. Closure of Perforated Ulcers

A. Simple Closure. (Fig. IIIA.)
B. Closure with Gastro-enterostomy. (Fig. IIIB.)

The most serious type of duodenal ulcer is one which has perforated into the peritoneal cavity. There were eight perforated ulcers in our series, all located in the duodenum within a few centimeters of the pylorus. A calloused indurated area two or three centimeters across usually surrounded the point of perforation. The problem which confronts the surgeon at the time of operation is whether simple closure shall be done or whether a gastro-enterostomy shall be done in addition to the closure. In making a decision we were influenced by three factors: the first, the length of time that elapsed between perforation and operation—after six hours a gastro-enterostomy was not done; the second, the risk of operation as determined by the age and general condition of the patient; and the third, the degree of obstruction in the duodenum caused by the closure of the perforation.

Technique (Fig. IIIA, B): A purse-string suture of catgut is passed around the ulcer and drawn sufficiently tight to close the perforation. Interrupted mattress sutures, usually three, are placed and tied so as to infold the purse-string suture. Omental tabs are sutured over the closure. If a gastro-enterostomy is added, it is done according to the conditions prescribed above.

Discussion: Acute perforation of a duodenal ulcer was first described by Joseph Penada of Padua in 1793. Mikulicz advised simple suture of perforated ulcer in 1880, and this was first done successfully by Heussner in 1892. Moynihan suggested adding gastro-enterostomy to simple closure in 1901. In our series four were treated by simple closure, and four by closure with gastro-enterostomy. Those who advocate the addition of gastro-enterostomy, usually limit this step to those cases which are operated upon within six hours of perforation, because a simple chemical and irritant peritonitis changes then to a septic type of peritonitis. The mortality rate increases directly as the time between perforation and operation increases. It varies from six per cent after operation within ten hours, to sixty per cent for operation after thirty hours. One perforation in our group of eight died. It was a case which had been perforated ten hours at the time of operation, a simple closure was done but the patient developed a subdiaphragmatic abscess and died. Probably fifteen per cent of the ulcers treated by simple closure will require a subsequent operation for recurrence of symptoms. The incidence of gastrojejunal ulcer at the stoma of

gastro-enterostomies done at the time of operation is placed at about two per cent by most writers.

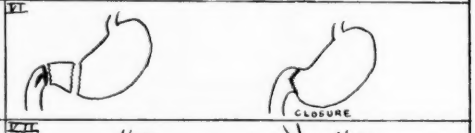
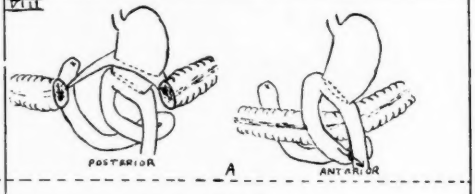
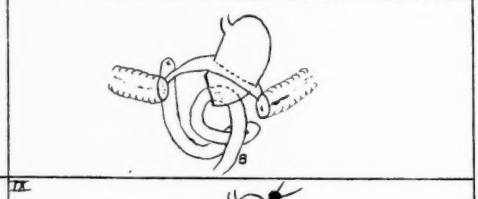
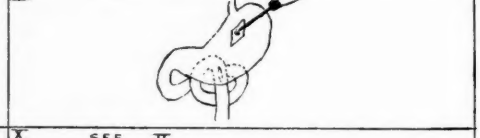
IV. *Devine Resection by Exclusion*

The next most complicated group of duodenal ulcers is the type of cicatricial lesion described above which is complicated by hemorrhage or threatened perforation. Such a lesion, associated with a patulous pylorus, would not be protected adequately by gastro-enterostomy. After a gastro-enterostomy, enough irritating chyme would pass through the patent pylorus to irritate the ulcer and prevent its healing, and possibly result in perforation or hemorrhage. These dangers are not, however, so imminent as to warrant extensive resection for all such lesions. A satisfactory compromise with adequate protection is afforded by the Devine operation, or resection by exclusion.

Technique (Fig. IV): This operation approaches the types of radical resections to be described later. The stomach is transected along an oblique line from the angle of the lesser curvature to a point proximal to it on the greater curvature. The distal opening is closed by a continuous suture, and infolded by a seromuscular suture, thus excluding the antrum and duodenum from the food stream. The proximal cut end of the fundus is sutured to the jejunum in one of four ways; the open end of the fundus may be anastomosed directly to the side of the jejunum as a retro-colic anastomosis, or as an anti-colic anastomosis with entero-enterostomy; or the open end of the fundus may be closed and the jejunum brought up and anastomosed side to side as either a posterior or anterior gastro-enterostomy.

Discussion: This operation was first reported by Devine in 1925. It has been used by many surgeons since then, and recently Lahey[4] recommended it as an operation of value for bleeding duodenal ulcers which require operation. We used it for two cases in our series. One was a patient who had recovered spontaneously from a perforated ulcer, and who had suffered a severe hemorrhage with threat of a second perforation. The other patient had a deep penetrating, bleeding crater ulcer associated with a large duodenal diverticulum and patulous pylorus. Neither case would have been protected adequately by a gastro-enterostomy, and each was too poor a risk for radical resection. The resection by exclusion solved both problems satisfactorily. Devine claims the same advantages for his operation, as for the more radical resections, but with less risk. There is a great reduction in the concentration of the acid; the stomach empties more rapidly; and there is freedom from unpleasant after-effects. Two patients on whom Devine performed this operation were reoperated by him in about twelve

GASTRIC ULCER 12 OPERATIONS.

TYPE OF OPERATION	NO	TYPE ULCER	TECHNICAL FACTORS	DIAGRAM
X PYLOROPLASTY	1	SMALL ANTERIOR PREPYLORIC	MOBILE DUODENUM NO CICATRICES	X SEE I
VI PYLORECTOMY BILLROTH I (HORSLEY)	2	DISTAL HALF ANTRUM		VI 
VII EXCISION (CAUTERY) AND GASTROENTEROSTOMY	1	ULCER AT ANGLE OF STOMACH	SMALL ULCER	VII
VIII PARTIAL RESECTION A. POLYA	2	PROXIMAL HALF ANTRUM GASTRIC AND DUODENAL ULCER		VIII 
B BILLROTH II	1	SAME	LARGE DILATED FUNDUS WIDE RESECTION SMALL POUCH	
IX TRANSGASTRIC CAUTERY AND GASTROENTEROSTOMY	1	ULCER FUNDUS POSTERIOR WALL		IX 
X GASTROENTEROSTOMY HIGH CARDIAC ULCER	4		BEYOND CAUTERY OR RESECTION	X SEE II

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months, and he found the excluded antrum contracted and empty. We made a similar observation on one of our cases upon whom we reoperated a year later. Studies on experimental animals have shown that the excluded antrum atrophies and becomes functionless. Devine claims excellent results in forty cases which were treated in this fashion.

GASTRIC ULCER

As the location of an ulcer shifts from the duodenal to the gastric side of the pylorus, the variety and extent of the operative procedures necessary to cope with it increase. This is due to the necessity of removing or destroying all chronic gastric ulcers, as ten to fifteen per cent of them probably undergo malignant change.

V. *Pyloroplasty*

This very conservative procedure is applicable in the very few instances in which the gastric ulcer is located on the anterior wall of the stomach close to the pylorus. We could use it for only one gastric ulcer in our series.

VI. *Pylorectomy: Billroth I*

Ulcers located in the distal half of the antrum but too far proximal from the pylorus to be suited for excision and plastic repair, are best treated by pylorectomy. This operation, as devised by Billroth, consists in removal of a sleeve of tissue from the stomach between the pylorus and a point proximal to the lesion, and uniting the stomach and duodenum in direct continuity.

Technique (Fig. VI): The pyloric and right epiploic vessels are ligated at the pylorus. A crushing clamp is placed across the pylorus and a non-crushing clamp across the first portion of the duodenum, which is transected between them. The gastrohepatic and gastrocolic omenta are ligated in sections over to the line of transection proximal to the ulcer. Here the vessels at the lesser and greater curvatures are ligated and the stomach transected between two clamps. With the ulcer-bearing area thus removed, the open end of the fundus is approximated to the open end of the duodenum, and they are anastomosed end to end. The posterior serosal surfaces are first sutured together by a continuous catgut suture. The posterior edges of the two openings are then sutured together by a through and through continuous catgut suture. This is continued anteriorly to approximate the mucosal layers, thus establishing the stoma of the anastomosis. The posterior seromuscular suture line is then continued anteriorly infolding the mucosal suture line. If the opening of the duodenum is too small to unite to the opening in the stomach accurately, the anterior wall of the duodenum may be slit longitudinally for a distance sufficient to compensate for the discrepancy in the circumferences. The completed suture line is protected by omental tabs.

Discussion: Resection of the stomach antedates the more conservative operations of pyloroplasty and gastro-enterostomy. In 1810 Merren of Giesen resected the pylorus of dogs, giving credit for the idea to an unnamed Philadelphia surgeon. Prior to 1877 Gussenbauer and von Winiwater, also Czerny and Kaiser, had successfully resected the stomach of dogs. In 1879 Péan, the great French surgeon, resected the stomach of a man for the first time. The patient survived for five days. In 1880 Rydigier, influenced by the experimental work of Gussenbauer and von Winiwater, of Wehr, and by the experience of Péan, performed the second unsuccessful resection of the pylorus in man. In 1881 Billroth reported the first successful resection done on a man, for carcinoma of the pylorus. In the same year Rydigier treated a large ulcer of the posterior wall of the stomach by resection, seventeen years before the first gastro-enterostomy was done for an ulcer. In 1903 Rodman suggested pylorectomy for all gastric ulcers, to remove the ulcer-bearing area of the stomach. We found the Billroth I operation best suited to two cases of gastric ulcer in our series. It represents the most physiologic of the more radical operations on the stomach, because the direct continuity of the tract is maintained, and the contents of the stomach are emptied directly into the duodenum as before operation. The results are satisfactory in ninety per cent of cases, with an occasional recurrence of ulceration or stenosis at the suture line.

VII. *Local Excision (Cauterization) and Gastro-enterostomy*

Ulcers located higher on the lesser curvature near the incisura angularis are more amenable to direct surgical attack than ulcers located elsewhere in the stomach. Formerly a sleeve resection of tissue containing the ulcer was made from the whole circumference of the stomach, and the open ends anastomosed in direct continuity. This operation has been abandoned because of the subsequent disturbance in the motility of the stomach, and the occurrence of hour-glass contractures at the suture line. Excellent results have been obtained by local excision of such an ulcer and the addition of a gastro-enterostomy. One case of gastric ulcer which we treated in this manner had bled before operation and was a poor risk for resection.

Technique (Fig. VII): The stomach is delivered well from the abdomen. The gastrohepatic omentum is dissected free from the ulcerated area, and if necessary the pyloric and coronary vessels are ligated on each side of the ulcer. Two V shaped segments of tissue are excised, one from the anterior wall and one from the posterior wall, the base of each meeting at the lesser curvature so as to include the ulcer. The two edges of the V on the anterior wall are approximated and also those on the posterior wall, and the mucosal edges sutured together by a continuous catgut suture. A seromuscular suture infolds the first suture line. The gastrohepatic omentum is sutured back in place. If preferable the ulcer may be destroyed by cautery, burning well out into the surrounding healthy tissue. The defect is

then closed and covered by omental tabs. Whichever procedure is used, it should be followed by a gastro-enterostomy.

Discussion: This method is less formidable then a radical resection, and meets satisfactorily the requirements of the situation. Balfour (1914) first suggested the destruction of such ulcers by the cautery, but it has the disadvantage that it destroys the specimen for pathologic examination. Local excision or cautery destruction alone does not suffice, because of the consequent disturbance of motility, and the high incidence of recurrent ulcers. A gastro-enterostomy is necessary to avoid disturbance in the mechanism of the emptying of the stomach. This combination has proved so satisfactory that Balfour considers it the operation of choice for ulcers at the angle of the stomach.

VIII. *Partial Gastric Resection*

A. Polya (Reichel and Balfour). (Fig. VIIIA).
B. Billroth II (Fig. VIIIB).

Frequently an ulcer will be so situated in the proximal half of the antrum that it cannot be removed by the methods described above. For an extensive lesion in the proximal half of the antrum, or for an antral lesion associated with a duodenal ulcer, both of which are to be removed, a more adequate resection becomes necessary. The two types of procedures we used in such situations were the Polya or Billroth II types. In the Polya type a wide sleeve of stomach wall between the fundus and the pylorus is resected, and the open end of the fundus is sutured to the side of the jejunum. In the Billroth II type, the same wide resection is made, but the stump of fundus is closed, and the jejunum is brought up and anastomosed to the fundus as a gastro-enterostomy.

Technique—Polya (Fig. VIIIA): The stomach is delivered and the proximal line of resection determined near the angle of the stomach. Two and a half centimeters proximal to where this proximal line crosses the lesser and greater curvatures the vessels are doubly ligated and cut. From this point the gastrohepatic omentum and the gastrocolic omentum are tied off in sections from left to right, over to the first part of the duodenum. The duodenum is transected between crushing clamps. The duodenum is closed by a running suture over the clamp, which inverts it as the clamp is removed. An additional serosal suture line inverts the closed end more completely, and it is covered with omental fat or sutured to the pancreas. The proximal crushing clamp at the pylorus is turned over to the left elevating the antrum and exposing the posterior wall of the stomach. In the Reichel method of anastomosis the jejunum is brought up through a rent in the mesocolon and approximated to the posterior surface of the stomach so that the proximal end of the jejunum meets the lesser curvature. A seromuscular suture line unites the jejunum and posterior wall of the stomach proximal to the line of resection at the antrum. The stomach is cut across one and a half centimeters distal to the suture line, thus removing the whole antrum of the stomach. The jejunum is then opened for a distance corresponding to the opening in the stomach. The inner mucosal layers of the stomach and jejunum are sutured together by a continuous through and through catgut suture. This is continued anteriorly, suturing the outer mucosal layers of the stomach and jejunum, thus establishing the anastomotic opening. The posterior seromuscular suture line is continued anteriorly, infolding the anterior mucosal suture line. When this anastomosis is completed, the bowel and stomach are drawn down through a rent in the mesocolon, and the edges of the rent are fixed high on the stomach with interrupted sutures. This is Reichel's modification.

Balfour suggests a long loop anterior anastomosis with an entero-enterostomy, instead of this retrocolic type which is frequently impossible without tension. The resection is carried out as above to the point where the anastomosis between the jejunum and stomach is ready. As described under anterior gastro-enterostomy the jejunum is adjusted so that it swings in front of the omentum and colon without tension, and is approximated to the posterior surface of the stomach. The resection of the antrum and the anastomosis of the jejunum to the stomach are carried out as described above for the Reichel type of retrocolic anastomosis. An entero-enterostomy between the afferent and efferent loops of the jejunum is made as described under anterior gastro-enterostomy. If in either type of anastomosis the opening in the fundus is too large to be used for a stoma, this may be circumvented by closing a quarter of the opening of the fundus at the lesser curvature end, and using the remaining three-quarters of the opening for the anastomosis, as suggested first by Hoffmeister.

Technique—Billroth II (Fig. VIIIB): This method affords another way than Hoffmeister's, for anastomosing a fundus with a large opening, to the jejunum. The resection of the antrum is carried out as described for the Polya, as far as the complete closure of the duodenum. Two large Payr clamps are placed across the stomach at the proximal line of resection, and the stomach is cut between them. This removes the antrum. The stump of the stomach in the proximal clamp is turned up with the transverse colon and omentum. An opening is made in the transverse mesocolon, and a gastro-jejunostomy done with the jejunum applied vertically to the posterior wall of the stomach. The anastomosis may also be made as a long loop anterior type with entero-enterostomy. The cut end of the fundus is closed by a running suture over the clamp, which inverts the stomach when the clamp is removed. This is reinforced by a second inverting seromuscular suture, and the whole is protected by covering the suture line with the lesser omentum.

Discussion: Billroth introduced partial gastrectomy in the form of his Billroth I pylorectomy in 1881, and introduced his Billroth II modification in 1883 to avoid the fatal leaking angle at the lesser curvature portion of the suture line in his number I method. The modification of the gastrojejunal anastomosis whereby the open end of the stomach was implanted into the side of the jejunum by the retrocolic route was introduced by Reichel in 1908, and independently by Polya in 1911. The Reichel-Polya re-

trocolic anastomosis was modified to an anticolic type with entero-enterostomy between the afferent and efferent loops by Balfour in 1917. We used the Polya types of anastomoses in two of our resections, one of which was done after reducing the lumen of the open stomach by the Hoffmeister method. We used the Billroth II anastomosis in one case with an extensive resection which left a small sac of fundus with such a large opening, that closure of the end of the stomach and side to side anastomosis of the stomach and jejunum offered the most satisfactory type of anastomosis. Such resections besides removing the ulcer-bearing portion of the stomach establish a low acidity and have as a consequence a lowered incidence of gastrojejunal ulcer. These more radical operations do carry a higher mortality rate, thirteen to fifteen per cent, than the more conservative operations, and for this reason are not the operations of choice for all benign gastric and duodenal ulcers.

IX. *Transgastric Cauterization and Gastro-enterostomy*

As the site of the ulcer moves from the angle of the stomach into the poorly accessible parts of the stomach, as on the posterior wall of the fundus, the danger of radical resection far outweighs any potential danger from the lesion itself. More conservative methods may be used to cope with them. An ulcer of the posterior wall of the fundus may be excised, or may be destroyed by transgastric cauterization, through an incision in the anterior wall of the stomach. Either procedure should be followed by a gastro-enterostomy. In our series one such posterior wall ulcer of the fundus which had recurred after a year of intensive medical treatment, was handled in this manner.

Technique (Fig. IX): The stomach is delivered from the abdomen. An incision is made high in the anterior wall of the fundus in its longitudinal axis, and overlying the ulcer on the posterior wall. The ulcer is excised or surrounded by moist packs and cauterized until its base is destroyed and the mucosal edges around the crater are freed. Deep catgut sutures are laid from one side of the ulcer to the other, so that when tied, the edges of the mucosa are approximated. The incision in the anterior wall of the stomach is closed, and the procedure is completed by the addition of a gastro-enterostomy according to the principles prescribed.

Discussion: The transgastric excision of posterior wall ulcers was popularized by W. J. Mayo. Their destruction by cautery, popularized by Balfour, is a technical modification of the procedure. The results are very satisfactory.

X. *Gastroenterostomy for Ulcers of Cardia*

The ulcers most difficult of access are those located high in the cardia near the esophagus. Here they are not resectable, or amenable to destruction by cautery with any degree of safety. However this type of lesion will respond satisfactorily to simple gastro-enterostomy. The literature conveys the impression that ulcers located proximal to the point of gastro-enterostomy will not heal satisfactorily. This has not been the experience of many competent observers. These ulcers of the cardia have responded satisfactorily to gastro-enterostomy in seventy per cent of cases. In very intractable ulcers of this type, Balfour suggests jejunostomy for complete rest of the stomach. We had four such ulcers in our series, and all have responded satisfactorily to simple gastro-enterostomy. One case in particular that we have seen frequently for a period of two years following operation, obtained immediate and complete relief from constant incapacitating pain of several years' duration.

GASTROJEJUNAL ULCERS

This group represents secondary lesions initiated by and developing after an operation for a primary ulcer. A gastrojejunal ulcer is a new and distinct ulceration at the site of a gastrojejunal anastomosis, and a gastro-jejuno-colic fistula is the complicating erosion of such an ulcer into the colon. The management of such lesions present the most complicated technical problems in the surgery of peptic ulcer. Depending upon the conditions present the steps consist essentially in disconnecting the gastroenterostomy, excising the ulcer and doing such a type of gastrointestinal anastomosis as is indicated.

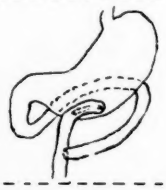
XI. *Disconnection of Gastroenterostomy and—*
- A. Polya or Billroth Resection.
- B. Polya or Billroth Resection.
- C. Roux en Y anastomosis.

Occasionally it will be found after disconnecting a gastroenterostomy and excising the jejunal ulcer that the duodenal ulcer for which the anastomosis was originally made has healed. Nothing further need be done except to close the defects in the stomach and jejunum. Subsequently the patient's diet should be regulated. Sometimes after disconnection of the anastomosis, a small ulcer of the duodenum will be found which is suitable for excision. One case in our series was treated in this manner with excision of the ulcer and a plastic repair, following closure of the defects in the stomach and jejunum. The method of choice, however, is to follow disconnection of the anastomosis by a partial gastric resection, which will minimize the likelihood of further ulceration.

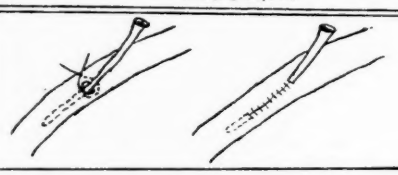
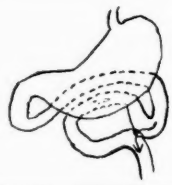
Technique: The stomach, colon and omentum are elevated and rotated on a transverse axis until the anastomosis between the jejunum and stomach is exposed. The mesocolon is freed from the posterior surface of the stomach where it was fixed around the line of anastomosis. The posterior wall of the stomach is caught on each side of the anastomosis with Allis clamps, and

pulled well down through the reëstablished rent in the mesocolon. A circular incision is made in the wall of the stomach surrounding the line of anastomosis, so as to remove a cuff of the stomach wall about a half inch in width. A rubber-covered clamp placed across the posterior stomach wall above the anastomosis, keeps the field clean. A ring of jejunal tissue of sufficient width to include the ulcer, is cut from the anastomosed portion of the mobilized jejunum. These steps remove a napkin ring piece of tissue, composed of gastric and jejunal tissue at the anastomotic line, and the ulcer. If no further resection of the stomach is to be made, the defect in the stomach is closed by two inverting suture lines. The defect in the jejunum is closed in a transverse direction by two rows of continuous catgut. If further surgery is necessary, either a pyloroplasty or a partial gastrectomy is done according to the indications and according to the principles discussed under each operation.

GASTRO-JEJUNAL ULCER 2 OPERATIONS

TYPE OF OPERATION	NO	TYPE ULCER	TECHNICAL FACTORS	DIAGRAM
XI DISCONNECTION AND GASTROENTEROSTOMY A. PYLOROPLASTY	1	JEJUNAL ULCER SMALL ULCER DUODENUM	MOBILE DUODENUM NO CICATRICES	XI SEE L
B. ROUX EN Y	1	JEJUNAL ULCER JEJUNO-COLIC FISTULA OBSTRUCTED PYLORUS DANGEROUS RISK	DUODENUM FIXED DRAINAGE NECESSARY	
C. POLYA	0	SAME		SEE VIII A

ACCESSORY OPERATIONS

TYPE OF OPERATION	NO	TYPE	DIAGRAM
XII JEJUNOSTOMY	2	POOR RISK VICIOUS CIRCLE	
XIII ENTERO-ENTEROSTOMY	1	VICIOUS CIRCLE	 J. C. McCANN

Occasionally a Roux en Y operation will solve a difficult problem after an old anastomosis has been disconnected. We used it on a fifty-five year old man with a gastro-jejunal ulcer and jejunocolic fistula, who was admitted to the hospital following a severe hemorrhage. There was a persistent complete pyloric obstruction, for which the original gastro-enterostomy had been done. After resection of the anastomosis and ulcer, there was absolute need for further surgery, but it was apparent that the patient would not survive a partial gastrectomy. A Roux en Y anastomosis was made as quickly as possible.

Technique (Fig. XIB): The gastro-enterostomy was disconnected in the manner described. The fistula into the colon was closed by a purse-string catgut suture. It was infolded by another suture line and covered with omentum. Six inches of inflamed thickened jejunum in the region of the ulcer had to be resected. The distal segment of the jejunum was drawn up to the anterior surface of the stomach and its cut end was closed by two rows of inverting sutures. The now closed distal loop was anastomosed to the anterior surface of the stomach in the form of an anterior gastro-enterostomy. The open end of the proximal segment of jejunum was brought over to the side of the distal segment below where it hung from the stomach. The cut end of the proximal loop was then anastomosed to the side of the distal loop three to four inches below the line of anastomosis to the stomach, thus draining the bile and pancreatic juice into the jejunum below the point of anastomosis.

Discussion: Roux introduced this type of operation in 1897 to eliminate the fatal vicious circle of vomiting which was fairly common with the early long loop types of anastomosis. This complication has been practically eliminated by the posterior short loop type of anastomosis now used. The Roux operation is not widely used as it is not sound physiologically. The gastric juice of full acid strength is poured directly onto the jejunal mucosa deprived of the usual protection of the alkaline bile and pancreatic juice. In a gastroenterostomy these juices flow down over the anastomotic area from above, but after the

Roux en Y anastomosis they enter the bowel four inches below the line of anastomosis. As a consequence this type of operation is followed by gastrojejunal ulcer in too high a percentage of cases to warrant its use. However it is a valuable emergency operation in some situations, and as Dr. Balfour once remarked "it is an operation that will get you out of a tight place."

ACCESSORY OPERATIONS

There are two operations which do not aim directly at the control of an ulcer itself, but which are of great value in meeting emergency situations which occasionally arise in the general surgical management of peptic ulcer. These are jejunostomy and entero-entero-anastomosis.

XII. *Jejunostomy*

Witzel introduced the principle of suturing a catheter into the gastrointestinal tract in 1891. We used it once to improve the condition of an emaciated patient who came to the hospital vomiting excessively from a mal-functioning gastroenterostomy performed elsewhere. Balfour recommends it for large ulcers high in the cardia, or for large inflammatory gastrojejunal ulcers which cannot be safely resected. It might also be used for late vomiting after gastroenterostomy due to closure of the stoma from porky inflammatory edema of the anastomosed stomach and jejunum, and mesocolon. We have observed this phenomenon once.

Technique (Fig. XII): A loop of jejunum is selected at a suitable distance from the duodenojejunal flexure. A purse-string suture about a half inch in diameter is passed on the antimesenteric border of the bowel. The bowel is perforated within the suture, and an 18 F catheter inserted for four to six inches. The purse-string suture is pulled tightly and tied. The catheter is laid longitudinally along the bowel wall proximal to the point of insertion, and the bowel wall approximated from each side over the catheter for about an inch. Two linen sutures are passed through the walls of the bowel over the catheter, and brought up on each side of the incision through all layers of the abdominal wall. After the peritoneum, fascia, and skin have been sutured in the usual way, the linen sutures are drawn tightly and tied, thus fixing the loop of bowel firmly to the abdominal wall, and preventing its slipping away from the catheter.

XIII. *Entero-Entero-Anastomosis.*

This operation was first introduced by Braun in 1892, who used it to unite the afferent and efferent loops of a long loop gastroenterostomy. It is also occasionally of value between the two loops of a short loop posterior gastro-enterostomy when the vomiting of a vicious circle appears. Although this complication has almost disappeared with the short loop anastomosis, yet it occasionally does develop. If due to the mechanical conditions of the anastomosis and not to inflammatory edema at the stoma, it may be corrected by enteroenterostomy.

Technique (Fig. XIII): The site of the anastomosis is carefully examined to rule out inflammatory occlusion of the stoma, in which case a jejunostomy will best tide the patient over until the edema subsides and emptying will correct itself. The duodenojejunal loop proximal to the gastro-enterostomy (afferent), is approximated to the jejunal loop that drains away from the stomach (efferent). An anastomosis is made between these two loops as described under the anterior gastro-enterostomy. This will drain the gastric and duodenal secretions across into the distal loop, thus preventing a vicious circling through the stomach and proximal loop. This is done when repeated lavage has failed to control the retention, and while the condition of the patient is still sufficiently good to withstand a second operation.

CONCLUSION

Technical methods used in the surgical treatment of ulcer are highly standardized, but the application of these methods to each ulcer must be made on an individual basis. The selection of the type of operation should be made when the ulcer is exposed at the operating table. The school of radical surgery advocates resection of the stomach for all benign ulcerations of the duodenum, with a general mortality rate of thirteen to fifteen per cent. The conservative school, to which most American surgeons adhere, advocates primary conservative surgical measures, to be followed by radical methods in the few cases that have unfavorable results. The mortality rate for conservative methods is probably half that of radical methods.

A study of 105 consecutive cases operated upon according to the precepts of the conservative school show that we employed the method of direct removal of the ulcer and subsequent pyloroplasty in eight per cent of the cases. Pyloroplasty was limited to small anterior wall juxtapyloric ulcers with a mobile duodenum that permitted of a plastic repair without tension. Posterior wall "kissing ulcers" with such anterior wall ulcers were destroyed by cautery. This procedure is ideal for bleeding ulcers when it is advisable technically.

Seventy-five per cent of the ulcers in this series were treated indirectly by gastro-enterostomy. This method leaves the ulcer in situ, but induces healing by side-tracking a portion of the food stream. This shortens the emptying time of the stomach, and reduces the acidity of the gastric juice, factors shown by experimental studies of the author[5] to be significant in causing chronicity of ulcers. We performed gastroenterostomy for unexcisable duodenal ulcers; after closure of some perforated ulcers; also as an additional procedure after excision or cauterization of gastric ulcers; and for unresectable ulcers high in the cardiac portion of the stomach.

For chronic bleeding duodenal ulcers in the presence of a patulous pylorus, the Devine resection by exclusion was used in two per cent of the series. By this method the same desirable

results which follow radical resection are attained and with less risk. We propose to use this operation for bleeding ulcers more extensively in the future.

Radical surgery was used for fifteen per cent of the cases. All gastric ulcers which did not heal on a medical régime were removed. Ulcers in the antrum of the stomach which could not be excised or destroyed by cautery were subjected to pylorectomy or partial gastrectomy. The two recurrent jejunal ulcers were treated, after resection of the jejunum, by pyloroplasty and a Roux en Y anastomosis respectively.

American clinics report eighty to ninety per cent satisfactory results after conservative surgical treatment of ulcers. The primary mortality rate is variable depending on many factors—climate, physical condition and nutritional state of the patient, and complications. The mortality rate reported by various surgeons is 2.5 per cent (Balfour[6], Mayo Clinic), 7.5 per cent (Pool[7], New York), 8 per cent, (Peck[8], New York), 10.8 per cent (Gibbon[9], Philadelphia), 15 per cent (Fordyce St. John[10], New York). Our series was operated upon with a mortality of 7.7 per cent. The deaths were chiefly from pulmonary complications in the group of difficult gastro-enterostomies.

This series, though small, illustrates the variety of operative procedures a surgeon should use if he is to meet properly the problems presented in the field of surgical treatment of peptic ulcer. Conservative surgery properly applied, will bring relief to many chronic invalids who do not respond satisfactorily to medical management. This can be done with a mortality rate which will not exceed the death rate for an average group of inadequately treated ambulant patients who roam our streets harboring dangerous chronic ulcers.

REFERENCES

1 Brown, R. C.: The results of medical treatment of peptic ulcer. J. A. M. A. 95: 1144, 1930.
2 Nielson: Quoted by A. A. Berg. The mortality and late results of subtotal gastrectomy for the radical cure of gastric and duodenal ulcer. Ann. Surg. 92: 340, 1930.
3 Judd, E. S., and Hazeltine, M. E.: The results of operation for excision of ulcer of the duodenum. Ann. Surg. 92: 563, 1930.
4 Lahey, F. H.: Discussion of paper by Allen. New Eng. J. Med. 208: 241, 1933.
5 McCann, J. C.: Experimental peptic ulcer. Arch. Surg. 19: 600, 1929.
6 Balfour, D. B.: Results of gastroenterostomy for ulcer of the duodenum and stomach. Ann. Surg. 92: 620, 1930.
7 Pool: Quoted by J. M. T. Finney, and E. M. Hanrahan, Jr. Results of operations for chronic gastric and duodenal ulceration. Ann. Surg. 92: 620, 1930.
8 Peck, C. H.: The present status of the surgical treatment of chronic duodenal and gastric ulcer. Ann. Surg. 80: 31, 1924.
9 Gibbon, J. H.: The immediate mortality in operations for gastric and duodenal and gastric ulcer. Ann. Surg. 92: 616, 1930.
10 St. John, F. B.: A follow-up study of the results in surgical therapy. Ann. Surg. 92: 597, 1930.

SOME PROBLEMS FREQUENTLY ENCOUNTERED IN THE TREATMENT OF RECENT FRACTURES*

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THE necessity for improved fracture treatment has been demanded in the last few years by the increasing number of fractures and their disabilities resulting from industry, automobiles, aeroplanes, and other technological changes. Even though many safety first methods and precautions have been introduced to lower the incidence of accidents, we can never entirely eliminate them, due mainly to the element of human carelessness. The aim of treatment is to expedite a complete recovery of function, which is best attained when the procedures run in harmony with the natural processes; that is, with powers of resistance, growth and repair.

The proper procedures in the early history of fracture treatment and the immediate recognition of all local and general pathology are important. Immediate splinting of the part involved regardless of the certainty of a fracture should be done. "Splint them where injured," thereby preventing unnecessary local trauma and shock. The benefit of splinting a fracture before transportation is attempted was demonstrated forcibly during the World War when the mortality rate was reduced in compound fractures of the femur from nearly eighty per cent to sixteen per cent after the adoption of this procedure. The splinting should be the simplest, most effective and most easily applied. Usually the simpler the splint the easier the application. In every case the joints which are proximal and distal to even the suspected fracture should be splinted.

The type of treatment depends on the individual case. Each fracture with its complications is a law unto itself, demanding individual common sense surgical judgment. The treatment should be adaptable to the fracture, the fracture must not be adapted to the treatment.

The writer does not believe that a standard method for the treatment of fractures in every case is possible. Not until every type of fracture can have the same bone and soft structure involvements, the same external force producing it, occurring in patients of the same age and having the same general physical and local conditions with the same resistance or recuperative power, can we hope to standardize the treatment of fractures. If this could be possible, treatment of fractures would cease to be a science and would not demand our own common sense judgment and expert opinion.

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Too frequently are superficial and careless physical examinations made, the results being that fractures are often overlooked. Certain cardinal physical signs are not always necessary to indicate a fracture. This is especially true in fractures of the spine where a patient may receive a slight or moderate fall on the buttocks, and afterwards suffer very little or no pain whatever in the spine, but when roentgenograms are taken a compressed fracture of one or more vertebrae is seen. A lateral roentgenogram of the spine when one suspects any bone involvement should always be made. We should always be suspicious of a fracture of the spine in even the slightest injury, directly or indirectly, to the back or buttocks.

In contrast to the above the case is presented which comes to the hospital unconscious as the result of a head injury, badly shocked, and showing every evidence of brain trauma. This patient should be treated symptomatically as a severe brain injury irrespective of bone findings. In cases of this type a roentgenogram frequently does not show a fracture of the skull. As a matter of fact roentgenograms in this type of case are not always immediately necessary for the proper treatment of the patient. Too often are patients with injury of such type moved to get roentgenograms, causing more damage than there is good derived from the knowledge obtained.

Roentgenograms, when possible, with anteroposterior and lateral views, should be made before attempting the reduction of a fracture. Following the reduction these same views as well as other roentgenograms at different intervals during convalescence should be made. These are not only necessary for checking up the position and union of the fracture, but as a protection and record for the doctor treating the case. When fluoroscopic examinations and reductions are done roentgenogram checks should also be made because fluoroscopic examinations cannot be recorded; such procedure, therefore, does no good before juries. Fractures cannot be treated by roentgenograms alone. The reduction of a fracture constitutes only one of the important processes in its treatment.

Early reduction should be done providing local and general symptoms permit. With certain severe fractures about joints, especially the ankle joint, with a large amount of swelling but good anatomical position, care should be exercised about placing such injury in a circular cast too early, with the possibility of cutting off circulation. Casts when applied should be cut along the whole course of application if there is any doubt whatever as to circulation. Of course, where the fragments are displaced they should be reduced as early as possible. If, however, when there is marked soft structure involvement and no fear of malposition developing, some simple wire or board splint should be applied with hot wet boric or saline dressings for twenty-four or forty-eight hours or longer (removing dressings every twelve or fourteen hours and inspecting them).

Relaxation during the reduction of a fracture is demanded. This relaxation can be accomplished by continued traction; massage; or spinal, local or general anesthesia, each one having its individual indications and advantages; however, no one method is to be used in every case.

Local anesthesia has taken a definitely indicated place with fracture work today, but it must not be used indiscriminately. It is not a panacea by any means. Harm can result from its use even though the enthusiasts say they have never had any trouble. The author prefers a one per cent novocain solution for local injection. Objections to local anesthesia are the following:

(a) When injecting the anesthetic, especially in fractures about the wrist joint, one gets a distortion of the landmarks; this, of course, is variable depending on the amount of anesthetic used.

(b) More pressure locally is brought about which prevents, to a certain extent, relaxation which would be conducive to manipulation and reduction.

(c) Theoretically, at least, the pressure from the injected local anesthetic impedes the blood supply.

(d) In certain cases the patient cannot be prevented from having some muscular rigidity.

(e) A latent spasticity of the muscles which seems to persist during convalescence more in the local anesthetic cases than when no local injections are used has been observed by the writers in several cases.

(f) The possibility of an infection, which would be a catastrophe but should not occur if proper technique is carried out.

The procedure of molding or kneading around fractures after injecting novocain or even when using general anesthesia in fracture reduction, especially about the ankle joint, seems to the writer a very dangerous procedure, being conducive to the formation of emboli and thrombi. Why bring about further trauma to already traumatized tissue as well as forcing traumatized blood into surrounding normal structures? Deaths and complications have been reported from such procedures.

The majority of all fractures can be reduced by the closed manipulative method and immobilized by circular or bivalved plaster casts. When doing the closed reduction, care must be taken that no serious local trauma is caused. Repeated attempts at closed manipulative reductions are not necessary before making a decision as to whether the continuous traction or open reduction technique is to be carried out in an individual case. Such type of treatment

by the closed method is not a conservative but a radical method of fracture treatment.

The writer believes that frequently more surgical judgment and care are demanded of the surgeon to be able to dextrously reduce a fracture by the closed procedure than by the open method. The surgeon who knows the anatomy, pathology and mechanics of the parts involved, the knowledge of which in the treatment of fractures is imperative, is able to do a closed reduction with minimum trauma. He is a more able surgeon than the one who cannot give such advantages, causing the patient to be subjected to unnecessary traumatizing closed reductions or open operative methods. Too tight bandages, splints or casts must never be applied. Frequent observation during the first few hours following the reduction of a fracture and every few days thereafter should be made. In any fracture living tissue is involved whether it be bones, muscles, ligaments, joints, nerves or blood vessels, any or all of which demand frequent attention, and without this observation undesirable results will usually occur. Fractures must not be tampered with too often; palpate only when necessary, but observe frequently.

The knowledge of the physiology of fracture repair and the surrounding soft structures is imperative. If we forget these we are not doctors treating fractures but mechanics, and will soon be in ill repute. Don't be like the physician who once asked me the following: "Doctor, the treating of a fracture is nothing more than a simple mechanical problem, isn't it?" We must also treat the general condition as well as the local pathology. Not infrequently examinations will show the cause of a fracture to be a certain bone pathology indicating a local manifestation of some constitutional disease existing before the fracture occurred.

There is now a wave of enthusiasm regarding the ambulatory treatment of fractures. No one believes in earlier motion in the treatment of fractures than the writer, but the laws of Hunter and Hilton on rest and immobilization must not be forgotten. Too early weight-bearing frequently brings about excessive painful callous formation and in certain instances nonunions and permanent disabilities. In certain fractures about the ankle joint with very little bone involvement and no displacement or any possibility of a displacement of the fragments, early weight-bearing soon after injury may be allowed provided a plaster splint and walking iron have been properly applied, and when supervision can be carried out frequently under ideal and controlled conditions.

The writer has concluded that the patient in the majority of such instances fortunately will control the overenthusiastic doctor who forces too early weight-bearing of the ankle and leg fractures, because of the pain which he encounters when carrying out such early weight-bearing. The common laws of nature generally will cry out for help against the faddism which is too often practiced by some members of the medical profession.

Even though the majority of fractures can be treated by the closed reduction method with fixation in some form of plaster splints or casts, with as early motion as is permissible, it is the minority in number which cannot be treated with this method and which usually make the majority in trouble. This minority demands, in most cases, our best judgment and opinion and represents probably the greatest difference in the proper and improper ways of treating fractures, resulting in the difference between excellent and poor results.

Skeletal traction treatment, which has usually been classified in the past as conservative, appears to the writer to be rapidly becoming a radical treatment. Too frequently are its limitations and indications being abused. The medical profession should not become overenthusiastic regarding the skeletal traction methods and assume that a panacea has been found for the treatment of all fractures. The writer still advocates and practices the use of skeletal traction in selected cases which in his opinion are ideal, and when indicated, application should be carried out without hesitancy. Rarely, if ever, are these selected cases in children, due to possible epiphyseal injury.

Skeletal traction has saved many extremities when properly used. The method demands close observation and patience. In the majority of instances, if used when indicated, good results will be obtained. Indiscriminate application of foreign material through the medullary canal should not be practiced. I prefer the Kirschner wire in the majority of instances due to its small size and its ease of application.

There are many types of tongs, pins, and wires which are good. Some have one advantage, others another; none is ideal. Better results are probably obtained by learning the use of one tong or pin thoroughly than by constantly changing as new ones are devised. It is inadvisable to use tongs with long points. They are apt to pierce too far into the bone.

The advantages of skeletal traction are as follows:

It is the only traction whereby one can get maximum traction with minimum application of traction material applied.

Since skeletal traction is direct, therefore, much less weight is required to overcome shortening.

Traction is regular and continuous, which it must be to be effective.

Properly applied, the method is entirely painless, and the patient is comfortable throughout the entire course of treatment.

The lower fragment is at all times under excellent control and can readily be brought into line with the upper one.

Since this leaves the rest of the limb entirely free, active and passive motions may be readily performed at the joints.

Open operation can be avoided in a large majority of cases.

Different types of physiotherapy treatments can be more easily applied.

Some of the disadvantages of skeletal traction are (1) the possibility of infection; (2) the introduction of foreign material through the medullary canal; (3) overextension of fragments which may cause a delayed or non-union, and (4) a rotation of the distal fragment if alignment is not frequently watched.

Adhesive plaster is in common use as skin traction and works well within limitations. A good grade of moleskin adhesive is preferable to zinc oxide adhesive.

Too prolonged traction should be guarded against because it brings about a varied period of temporary muscular paralysis which is difficult to overcome at times, and also, when using skeletal traction for too long a time infections are more liable to occur around or along the course of the wire or pin. As soon as alignment is restored and sufficient callus has formed and when some type of fixation can be applied, the skeletal or adhesive traction should be removed.

In certain selected cases where the economic status will not permit hospitalization it is not contraindicated to use a non-weight-bearing ambulatory plaster cast with skeletal traction and countertraction incorporated in the cast. Here again, however, this type of skeletal traction is not to be used indiscriminately; it is only indicated in a few cases, and such cases demand close observation. Excellent ambulatory traction and counter apparatus have been described by White, Carter and others.

Open operative reductions when indicated should be done without hesitation. The indications, however, for open operative reductions before first trying to do the reduction by the closed or traction methods are few. It is not necessary to discuss the technique of different types of internal fixation except to say that as in all other methods of fracture treatment the surgeon should use that recognized standard method with which he is most familiar, and if not familiar with such methods proper consultants should be obtained.

When delayed union is present be slow to call it non-union, because if surgical interference is carried out too soon in such types of cases the surgeon may be defeating the whole purpose and progress toward union. Frequently patience on the surgeon's part will be rewarded by union taking place. Generally speaking a delayed union is not a non-union until five or six months from the date of injury.

Too early weight-bearing after removal of all fixation, especially in fractures of the ankle or knee joint should be guarded against. Frequently fractures of the knee joint during early convalescence do not show any instability but, if walking is allowed too soon without a support, become unstable. The same is true of ankle fractures.

Physical therapy is essential in all fractures, not necessarily and entirely machine therapy, such as diathermy, but the use of the simple physical resources such as hot water and ordinary heat and lights.

Too prolonged fixation is a very disabling procedure. It is not conducive for early function. Early active motion used by the patient is one of the most important procedures in accomplishing good functional results. Hot and cold contrast baths are to be used when sufficient callus formation has taken place to allow the temporary removal of any fixation from the involved part. Massage and other forms of physiotherapy when accessible are of great help. All of these procedures should be under the direct supervision of the doctor treating the case, and when possible in coöperation with a capable physiotherapist of the medical profession.

In fractures with skeletal traction or a Thomas splint some form of radiant heat is useful, and the patient can often be instructed to give himself some superficial massage. The coöperation of nursing in physical therapy is essential. In hospitals where there are physiotherapy departments, the patient often gets the impression that all he must do to obtain function is to visit this department once daily. This, of course, is a tragic development.

The splinting in physiotherapy is too frequently overlooked. In a stiff shoulder with a weak deltoid and contracted pectoralis major, no physical therapy will produce function by an hour's treatment if the arm is allowed to hang for twenty-three hours instead of being in an aeroplane splint.

One of the most important physical agents to use in fractures is exercise. The muscles of the body are expected to work together in the coördinative movements which we use in our daily ordinary work and they will work together longer when there is a purposeful nature in the exercise. Therefore, curative occupational therapy is probably the best exercise and is of the greatest value. Even without expert directions the surgeon can with a little ingenuity use occupational therapy.

One's ability as a surgeon in treating fractures is not determined entirely by the method or methods of treatment which he uses but by the functional results obtained. The surgeon

behind the treatment is most important. Frequent observations during the convalescent period of a fracture are essential. The surgeon who reduced the fracture should realize that it is not beneath his dignity and responsibility to remove a cast or splint during convalescence and inspect an injured limb, and to reapply the splint, giving his opinion for future treatments. Good surgical judgment is just as necessary during the convalescence of a fracture as at the time of the reduction.

Ultimate results to be attained and hoped for in any fracture are union, alignment and function. When all other factors are equal, perfect bone approximation is usually conducive to early union and restoration of function. However, the possibility of obtaining good functional results when good alignment is present should never be sacrificed merely to obtain perfect bone approximation, because a return to normal function is not always dependent on perfect bone reapposition. This is mainly true in shaft fractures but usually not so in joint fractures where it is best to get as good anatomical position as possible to obtain good function. Finally, function is not only dependent upon union and alignment but also upon full coöperation and determination of the patient to aid himself during convalescence.

The psychologic aspect of the patient with a fracture is an individual problem. A thorough understanding by the patient as to his condition should be explained by the physician, and the patient assured that he will have an excellent chance to recover normal functions if such is at all possible. Due consideration should be given to the compensation case who generally has a longer disability than the corresponding injury in another patient. Confidence of the patient in the physician is essential.

CHANGE IN THE MASSACHUSETTS CANCER TREND*

BY GEORGE H. BIGELOW, M.D.,† AND HERBERT L. LOMBARD, M.D.†

IN a paper published in 1926[1] the committee studying the cancer situation in Massachusetts suggested that on the basis of the break in the trends in certain age specific groups the saturation point was not far distant. Schereschewsky[2], in 1925, suggested that cancer would be subject to the general law that physical, chemical and biological processes all tend to a state of equilibrium and that, as a result, its saturation point might be expected. The record of ten additional years has now been obtained with the result that the break in the trends is even more apparent. In all of the female age groups the trend is changing, and in those under seventy an actual downward tendency is noted. Among the males the change is present, although not marked. The break in the trends began at different periods in different age groups, and as similar phenomena have been noted in other diseases, it has been inferred that cancer might have a biologic rise and fall.

In addition, however, to what may be occurring in the disease itself, there has been during the past few years a concerted drive toward the control of cancer. The American Society for the Control of Cancer began its activities in 1913 and the Massachusetts Cancer Program was inaugurated in 1926.

In an attempt to determine the factors behind the changing trend, a study was made of the cancer death records in Massachusetts from 1900 to 1932 and of additional data obtained from the records of the Massachusetts State-aided cancer clinics and cancer hospital.

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Rates adjusted to age for males and females have been computed for individual years from 1900 to 1932 (table I). As a pronounced break in the trend in females occurred in 1916, trends prior and subsequent to this date have been obtained for both sexes. The trend for the males from 1900 to 1915 was +1.65, while from 1916 to 1932 it was +1.35. There is a slight, but not marked, lowering of the trend in the second period. Among females the two respective trends were +1.93 and +0.17. The drop in the female trend is significant and indicates some factors at work in this sex which are not present in the males.

The improvement among females is most apparent in the age groups under sixty. Between 1920 and 1930 the native born show a stationary trend among females, while the foreign-born show a downward trend. Among the males the trend is upward but is less among the foreign-born than the native born.

When the deaths are subdivided by location of cancer, among the males significant downward trends are noted only in cancer of the skin. Among the females, digestive tract cancer and cancer of the skin have significant decreases. In the nativity groups the only significant decrease is in digestive tract cancer among the foreign-born females. Breast cancer has a significant upward trend in the total group, but in the nativity groups is significant only in the native born of foreign and mixed parents. Although the trends of certain individual nativity groups are not significant the inference appears that skin cancer of both sexes is declining, that digestive tract cancer among the females is declining, that female genital cancer is about stationary, and that cancer of the breast is slightly increasing. A large part of the

improvement seems to lie among the foreign-born.

An increase in digestive tract cancer among males and a decrease in the same type among females does not seem reasonable. The International List of Causes of Death classifies the location of cancer by its place of origin. If the attending physicians are reporting today cancers by place of origin, while in previous years they reported similar cases by place of metastases, we would expect to find less improvement in breast and uterine cancer than actually occurs. It is reasonable to assume that such a change has occurred and that part of the seeming decrease in digestive tract cancer is apparent rather than real, and the rates for breast and female genital cancers are less than the figures indicate.

While we have no authentic figures to prove that such is the case, we know that at the present time many physicians are still reporting by organ of metastases. A study of 600 cancer records where the diagnosis was established at the Pondville State cancer hospital and where death occurred elsewhere showed radical changes in the organ affected. Of 149 cases certified on the death record as being due to cancer of the digestive tract, ten at Pondville had originally been diagnosed as cancer of the uterus, seven cancer of the breast, sixteen cancers of other sites, and twelve non-cancer. While it is admitted that the Pondville diagnosis may at times be in error, the fact is established that at the present time breast and uterus cases are being classified as cancers of the digestive tract. It is believed that this was done to a far greater extent in 1920 than at present.

Inasmuch as the greatest changes are appearing among the foreign-born, this group has been studied in detail. In a paper on Cancer Mortality in Nativity Groups[3], it was shown that the foreign-born and their children had higher rates for cancer than the native-born of native parents. The differences were particularly marked in cancers of the mouth and digestive tract.

The average age at time of death of the foreign-born with cancer was 63.6 years, and of the native-born of native parents, 68.3. A part of this difference may be due to the differences in the location of cancers, but the major part is assumed on the basis of our findings in other chronic diseases[4] to be due to earlier age of attack.

The duration of cancer among the foreign-born is shorter than is that of the native-born. A higher mortality, an earlier age of incidence, and a shorter duration might indicate either a greater virulence of the disease or less resistance among the foreign-born. This seems probable as the cancer clinic records show that the duration of symptoms prior to visit to the clinic is about the same among the foreign and native females and slightly less among the foreign males than the native males, but that the percentage complaining of pain when arriving at the clinic is greater among both sexes of the foreign-born than the native-born. As pain is usually a late symptom of cancer, it would seem reasonable to assume that when the foreign-born arrived at the clinics the disease had progressed more rapidly than it had among the native born.

Six months after admission to the clinics, twenty per cent of the foreign-born and only fourteen per cent of the native-born with four native grandparents were dead. At the end of eighteen months the figures were about 37 per cent and about 27 per cent, respectively. The question arises, "Do the foreign-born receive as adequate treatment as the native born?" Many of them attend the clinics in large hospitals where they are under the supervision of some of the best men of the profession.

Massachusetts is composed of 25 per cent foreign-born population, but the proportion of attendance in the State-aided cancer clinics is nearly 40 per cent foreign-born.

The percentage of the foreign-born who die with cancer having had a previous operation is slightly less than that of the native-born, but the number of unknowns is large and could easily alter the figures. On the basis of the death records, the foreign-born receive operations for breast and female genital cancer slightly earlier than the native-born. It would be hard to say from the data that the type of treatment received by the foreign-born was any less adequate than that received by the native-born.

It would seem that the change in the cancer trend is due to one or more of the following:

1. Cancer is reaching a saturation point in our population.
2. The concerted drive against the disease is lowering the trend.
3. The improvement is apparent rather than real, due to changes in diagnosis.
4. The changing composition of the population is altering the rate with no change in the disease itself.
5. Changing living habits may be contributing to the situation.

There are arguments for all five of these premises. If a saturation point is being reached, we might expect the change to be first noted in the groups having the highest rates. We find this. The changing of the trends at different intervals in different age sex groups would also point in this direction. Moreover, the first break in the trend occurred prior to the intensive work in cancer control.

The results from the concerted drive against

cancer might be accomplished by cures, by prevention through the removal of precancerous lesions, and by the prolongation of life in individuals not amenable to cure. If an increase in the number of cures can be attributed to the cancer campaign in this State, the effect would be felt in the death rate about two years later, the lapse being due to the average duration of cancer. The removal of precancerous lesions might be felt at any time after this two-year interval. It is impossible to judge, of course, which of these lesions if left alone will eventually become cancers or at what period. It is extremely doubtful if many of the precancers are at the point of developing cancer when treated, and such effect on the death rate would, therefore, be largely at a later period. Both an increase in the number of cures and removal of precancerous conditions would permanently lower the cancer rate. Methods used to prolong life but not to cure would have a tendency, at first, to lower the cancer rate, but would later contribute to a rise.

The results of programs for cancer control would be expected among the more accessible cancers. The greatest improvement is appearing among females who have more accessible cancers than males. The downward trend in middle-aged females points toward improvement in breast and uterine cancer, and if we assume that a part of the digestive tract cancer has been wrongly classified, the result would indicate that the rates for breast and uterine cancer have been lowered. Five years after the inauguration of the Massachusetts Cancer Program, the general hospitals in Massachusetts were admitting 34 per cent more cancer than before, while in parts of the United States where such programs had not been so intense, the increase was 21 per cent. The concerted drive against cancer has improved the type of treatment the patients receive. In the five-year interval there was a sixteen per cent decrease in cancer patients dying following operation in hospitals, and a 22 per cent decrease in patients dying following radiation in hospitals.

The number of patients attending the Massachusetts state-aided cancer clinics is increasing. In 1932 the total attendance was 254 per cent greater than in 1927, the number of individuals with cancer was 260 per cent greater, and the number with precancerous lesions was 344 per cent greater—the actual figures for 1932 being 3,427 total attendance, 793 with cancer, 303 with precancerous lesions. The median delay between first symptoms and visit to clinic has also decreased slightly for cancers of all locations, and over 30 per cent in breast and buccal cavity cancers.

While it is reasonable to assume that a part of the increase in cancer might be due to better diagnosis, it is more difficult to believe that a decrease could be accounted for by the same reasoning. Wells[5] reports an autopsy series in which he found 178 cases of cancer not so diagnosed and only thirty-three cases diagnosed cancer that were not cancer. Riechelmann[6] reported 711 cases, 156 not being recognized as cancer and only fifty-eight cases diagnosed as cancer with the disease not present. This would indicate that improved diagnosis would tend to augment, rather than depress, cancer rates. It may be utopianly argued that the increase has stopped by arriving at the maximum of diagnosis perfection, but still this does not account for a decrease. It would hardly be seriously advanced, we think, that the general accuracy of diagnosis throughout the State was deteriorating.

How important are mixed nativities in the changing cancer trend? The native-born of native parents are not an entity in themselves. The census does not furnish information as to the composition of their grandparents. Some of this group have American forebears since early colonial days, while others are the grandchildren of immigrants. We know that the children of the foreign-born have higher cancer rates than those of native-born parents and even than the foreign-born themselves[3]. We do not know whether this is carried on to successive generations. The foreign-born ranks are becoming more and more complex and it is reasonable to assume that the native-born of native parents of 1930 may differ considerably from this group at earlier periods. The composition of the foreign-born can be ascertained with a fair degree of reliability. Between 1920 and 1930 the proportion of Irish among the foreign-born has decreased from 17 per cent to 15 per cent, while the Italians have increased from 10.8 per cent to 12 per cent. The proportion of individuals born in Russia-Poland has decreased from 15.5 per cent to 13.3 per cent, while those born in Canada have increased from 24.2 per cent to 27.2 per cent. These four nativity groups comprise two-thirds of the foreign-born population in Massachusetts. The cancer rate among the Irish is high; among the Italians, low[3]. The Canadians and Russian-Polish group have moderately high rates. The change in the composition of these four races might alone decrease the cancer rate in the total foreign-born group.

The extent to which environmental factors contribute to cancer is problematic. Various types of irritation have been shown to be associated with the disease. Others have been postulated. There are probably countless irritations connected with diet, exercise, and other forms of daily behavior. These may predispose to cancer or they may not. Again, there have been profound industrial changes. With the practical disappearance of carpets, tacks no longer irritate under the tongues of those who used to lay them. There are many other changes that are more subtle. While largely theoretical, it is well known that there have been great

changes in the living habits of the people in recent years which might affect cancer predisposition. Individuals today are far more vitamin-conscious than they were a few years ago. Green vegetables are considered an all-year diet instead of a seasonal one. Greater attention has been given to personal hygiene. Clothing is more sanitary. On the other hand, the strain and stress of present-day life is more exacting than it was a generation back. How much this may have to do with the cancer problem cannot be answered, but it must be given consideration.

TABLE I

MASSACHUSETTS AGE, SEX ADJUSTED CANCER DEATH RATES

Adjusted to Massachusetts 1900 Population

Year	Rate per 100,000 Male	Female	Total
1900	50.2	91.6	71.5
1901	50.6	93.7	72.7
1902	47.9	97.0	73.0
1903	50.9	97.8	75.0
1904	54.2	102.9	79.2
1905	55.5	103.7	80.3
1906	63.1	99.5	81.8
1907	58.9	108.7	84.4
1908	59.9	108.7	84.9
1909	60.3	108.5	85.0
1910	63.7	111.3	88.1
1911	68.8	112.1	91.0
1912	63.5	117.6	91.3
1913	71.5	119.7	96.2
1914	70.9	119.6	95.9
1915	73.7	119.5	97.2
1916	77.1	126.5	102.5
1917	76.2	127.0	102.3
1918	78.6	123.2	101.5
1919	77.9	120.5	99.7
1920	84.5	128.6	107.1
1921	85.9	129.4	108.2
1922	83.5	126.9	105.8
1923	85.4	125.8	106.1
1924	92.2	127.5	110.3
1925	89.6	130.0	110.4
1926	94.3	127.5	111.4
1927	92.5	128.9	111.1
1928	94.3	128.8	112.0
1929	93.3	127.4	110.8
1930	96.8	125.4	111.5
1931	93.6	126.2	110.3
1932	97.1	129.1	113.5

The evaluation of these five possibilities leads us to believe that diagnosis is of least importance, that health habits should be considered but as yet there is little to warrant a belief in their importance in this matter, and that the other factors (more adequate and earlier treatment, changes in racial stock, and a saturation point in cancer being reached in our population) may have about equal weight.

CONCLUSIONS

The trend of cancer mortality in Massachusetts is changing with the curve flattening out and a slight decrease noted among females. The rate for the foreign-born females is decreasing faster than for the other groups. While the death rates indicate that cancer of the digestive tract in females has the greatest improvement, it is believed that erroneous classification in the earlier years is responsible and that the decrease is really in breast and uterine cancer. It is our opinion that the improvement in the cancer death rate is caused by the concerted drive against cancer, by changes in the composition of the foreign population, and by the possibility of a saturation point in cancer being reached.

The relative significance of each of these factors must be determined in the future, if at all.

REFERENCES

1 Nichols, John H.; Goodhue, Frank W.; Champion, Merrill E.; Bigelow, George H., and Lombard, Herbert L.: Cancer in Massachusetts. Boston M. & S. J. 194:388 (Mar. 4) 1926.

2 Schereschewsky, John W.: The course of cancer mortality in the ten original registration states for the 21-year period, 1900-1920. United States Public Health Bulletin, No. 155, 1925.

3 Lombard, Herbert L., and Doering, Carl R.: Cancer studies in Massachusetts. 3. Cancer mortality in nativity groups. The Journal of Preventive Medicine. 3:343 (Sept.) 1929.

4 Bigelow, George H., and Lombard, Herbert L.: Cancer and Other Chronic Diseases in Massachusetts. Boston and New York, Houghton Mifflin Co., 1933.

5 Wells, H. Gideon: Cancer statistics as they appear to a pathologist. J. A. M. A. 88:399 (Feb. 5) 1927.

6 Riechelmann, W.: Eine Krebsstatistik vom pathologisch-anatomischen Standpunkt. Berl. klin. Wchnschr. 39:728 and 758, 1902.

PERICARDIAL HEMORRHAGE COMPLICATING SCURVY*

A Case Report

BY WALTER E. BARTON, M.D.,† AND WILLIAM FREEMAN, M.D.†

SCURVY, Scorbutus, or Moeller-Barlow's Disease is due to the deficiency of a specific water-soluble vitamine, called "C." The history, etiology, clinical course, and pathological findings of this condition are too well-known to bear detailed repetition here. This information is readily accessible in any of the standard textbooks on the subject. In brief, the disease is generally divided into two major types, the infantile and adult, depending upon the age of the patient. The two groups are similar except that the bone changes in the infantile group are much more profound than in the adult. The outstanding symptoms and signs are irregular

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fever, weakness, and malaise; ecchymosis of the skin; swollen, spongy, and bleeding gums; subcutaneous, submucous, intramuscular, and subperiosteal hemorrhages of a greater or less magnitude. Bierich[1] tabulated the postmortem findings of the largest group of cases (over 1300). Erdheim[2] also reported the findings in a large series of cases that he personally examined.

Both Bierich and Erdheim emphasized the consistency of the hemorrhagic findings. In rare instances they found intrapleural or intra-abdominal hemorrhages. Bierich considered the bleeding due to an exogenous injury of the vessel wall after the wall was endogenously changed by the lack of the specific vitamine. Wolbach[3] felt that this endogenous change is brought about by the lack of, or change in the intercellular cement substance. Erdheim emphasized the importance of right cardiac hypertrophy, a finding that he obtained in over 67 per cent of his cases both in the infantile and adult types.

In a careful review of the literature as far back as 1910 no reference was found to an intrapericardial hemorrhage. It was on this account that the following case was considered to be of sufficient interest to warrant publication.

CASE RECORD: T. V., hospital number 33776, a forty-four year old white male was admitted to the Worcester State Hospital in 1917 and was subsequently given the psychiatric diagnosis of schizophrenia. He had definite hallucinations and delusions with frequent catatonic episodes. One of his frequent delusions was to the effect that food would injure and possibly kill him. On this account he frequently refused to eat. The remainder of the psychiatric data were irrelevant to the thesis on hand.

On May 29, 1931 (then 58 years of age) he was transferred to the Medical Service from a psychiatric ward, presenting hemorrhages from the gums and purpuric spots of the lower extremities. A careful check-up revealed the fact that this patient would, when left to his own choice, eat only meats and a very small amount of boiled potato.

Physical examination revealed a well-developed and well-nourished adult male. The essential findings were swollen and spongy gums that bled easily. The teeth were demarcated from the gum margins by blackened, necrotic areas. There were many purplish patches scattered over the buccal mucous membrane. The tonsils were buried and covered with grayish white follicular spots. There was a slight infection of the anterior pillars and posterior pharynx. The sublingual ducts and glands were reddened and swollen. On the right side of the neck there was one small, firm anterior cervical gland, the size of a marble. Moist crackling râles were found in the apices of both lungs. The skin was coarse and thickened with many dark chocolate brown macular areas over the lower extremities, abdomen and back, in many places becoming confluent and not fading on pressure. Pitting edema extended upwards to the mid-tibial regions in both legs. The pupils were sluggish in reaction to light and slightly irregular. There was a hordeolum of the right eye and a whitish discharge from the lateral commissure of the left eye. The heart findings were essentially normal. The blood pressure was 130/80 with a moderate beading of peripheral vessels. The abdomen was normal. The temperature was 99.8°F., pulse 80, and respirations 20.

Laboratory studies revealed the urine to contain a minute trace of albumen with finely and coarsely granular casts. A "Mosenthal" kidney function test showed a fixation in specific gravity between 1.008 and 1.012, with a total urine output of 618 cc., of which the night component was 250 cc., with a specific gravity of 1.012. The blood analysis revealed a N.P.N. of 44; Urea 30; Uric Acid 3.9; Creatinine 1.4, and Sugar 87 mgm. per 100 cc. of blood. Erythrocytes were 3,790,000, with anisocytochromia moderate; leucocytes 6,550; hemoglobin 80 per cent; neutrophils 72 per cent; and lymphocytes 28 per cent. The bleeding time was ½ minute; clotting time three minutes. The platelet count was 268,000 per cubic mm. of blood. A provisional diagnosis was made of scurvy with generalized arteriosclerosis and chronic nephritis with edema. Accordingly the patient was placed upon a special diet which included an abundance of fresh vegetables and orange juice daily. At the end of a week there was little change and the edema had extended to the knees. In another week the purpuric spots on the legs began to recede and the bleeding of the gums improved. The blood findings were essentially the same as before. X-ray examinations of the long bones revealed a general periosteal thickening with a little roughening.

Much difficulty was encountered because of the patient's poor coöperation in all kinds of therapy. Four days later he developed urinary retention and was catheterized. Rectal examination revealed a firm, hard, smooth, symmetrically enlarged prostate. During the next eight days he was catheterized daily and the residual urine gradually decreased. The general condition was markedly improved and the purpuric spots and edema had entirely disappeared. At this time the red count was 4,260,000 per cu. mm. On June 27 he was discharged back to the psychiatric wards as recovered. On October 5 (over four months later) he was readmitted with symptoms of faintness, cyanosis of the face, repeated coughing, nausea, and vomiting. Examination revealed the gums, mouth, and throat to be in the same condition as previously reported. His breath was cadaverous and lips cyanotic. This time the heart was noted to be moderately enlarged, one cm. outside the nipple line. The heart tones were only fair in quality and a soft, blowing, non-transmitted, presystolic murmur heard best at the tricuspid area was noted. The pulse pressure was of low tension and compressible. The blood pressure was 102/80. The liver edge was smooth, slightly tender and three finger-breadths below the costal margin. There were numerous small purpuric spots over the legs and trunk and a brownish pigmented area over the lower abdomen and another on the left ankle which appeared indurated. The temperature was 101.2°; pulse 88; and respirations 20 per minute. The urine was as before. The red blood count was 5,160,000; leucocytes 15,000; the remainder of the blood morphology was as before.

The patient vomited a small quantity of greenish fluid and did so again the next day. He became restless and refused to eat. It became necessary to feed him daily by nasal tube, a quart of eggnog and the juice of two oranges or its equivalent in tomato juice. There were no urinary disturbances at this time.

On October 11 his color suddenly became poor and respirations shallow. He was dyspneic and groaned, but could not localize his difficulty. The temperature was 103.6°; pulse 120; and respirations 20. The heart sounds became increasingly weaker but regular and the pulse remained steady. The chest findings were otherwise normal. The patient expired suddenly within two hours.

Postmortem Examination: The autopsy was performed 19 hours after death. The patient undoubtedly died of a pericardial hemorrhage, the pericardium containing 28 ounces of fluid and clotted blood. The epicardium was covered on all surfaces by many short, coarse, hemorrhagic, easily friable, fibrinous adhesions. Microscopical study showed organizing, hemorrhagic, fibrinous adhesions attached to the epicardium. A careful examination of the heart did not elicit any point of bleeding even after making thin, cross-section slices of the entire organ. The heart weighed 420 Gm., and measured 14.5 x 12 x 5.5 cm., thick. In addition to swollen, spongy, and bleeding gums, there was blood around the larger vessels of the subcutaneous tissues, submucosa of the gastro-intestinal tract and subperiosteum of the ends of both femurs. The medullary portion of the left adrenal was hemorrhagic and the central portions of the femoral bone marrows markedly congested. The vessels of all of the viscera were likewise injected. The remainder of the findings were insignificant.

DISCUSSION: One might be led to suppose that the epicardial hemorrhage occurred as a result of a general oozing from the walls of the coronary vessels, particularly those nearer the surface but this bleeding is more apt to be from epicardial and pericardial vessels, rather than from the coronaries.

The first question arises whether this was a case of scurvy. The most cogent argument is the fact that the patient recovered from the first attack after foods high in antiscorbutic vitamine content were forced. Due to the patient's mental condition and peculiar diet, when left to his own resources, the onset of scurvy was ever a possibility. The ecchymosis, gum bleeding, irregular fever and malaise are consistent with scurvy as are also the postmortem findings of bone marrow congestion; subperiosteal hemorrhages; hemorrhages about the vessels of the subcutaneous and submucous tissues; and congestion of the organs. All of the postmortem findings fit in better with scurvy than with any other diagnosis.

SUMMARY: A case is presented of a fifty-eight year old, white male schizophrenic patient who developed symptoms and signs associated with those found in scurvy or vitamine C deficiency. On a diet high in vitamine C, the patient soon recovered, but due to his mental condition, when left to his own resources, he again rapidly showed signs and symptoms identical with those of the first attack.

He died suddenly during the second attack of a massive intrapericardial hemorrhage which apparently came from a general oozing of the entire epicardium. With it were other findings usually accompanying the results of this deficiency disease, namely, irregular fever, malaise, bleeding from the gums, ecchymosis of the subcutaneous and submucous tissues, subperiosteal hemorrhages, and femoral bone marrow congestion.

CONCLUSIONS: This case emphasizes the necessity for careful watching of the diets of all mental patients in order to prevent the onset of any deficiency diseases. The cafeteria system of handling food which is rapidly coming into style in most mental hospitals and which permits the patient a greater choice of foods than was heretofore possible has the danger of developing bad dietary habits and increasing the incidence of deficiency diseases. Therefore, steps should be taken to correct this fault.

Intrapericardial hemorrhage may, in extremely rare instances, complicate scurvy.

REFERENCES

1 Bierich, R.: Ueber Skorbut. Deutsches Arch. f. klin. Med. 130:151, 1919.
2 Erdheim, J.: Ueber das Barlow-Herz. Wien klin. Wchnschr. 31:1293, 1918.
3 Wolbach, S. B.: Address before the Boston Pathological Society, 1932.

MEDICAL PROGRESS

PROGRESS IN HEMATOLOGY (1929-1933)*

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PROGRESS in hematology in the past five years has been astounding. Not since the days when Ehrlich first applied the techniques of the aniline-dye industry to the staining of blood cells has there been such intensive and extensive investigation of the disorders affecting the blood-forming organs. This has been due, in part at least, to the epoch-making discovery of Minot and Murphy, reported in 1926, that liver would cure a hitherto always fatal disease, pernicious anemia. Until this significant milestone, "blood" diseases were considered almost universally fatal and, to the average physician, of but little more than academic interest. Pernicious anemia began to be studied with feverish interest, and from these studies came many useful by-products.

Until fairly recently, there was no general recognition that the so-called "diseases of the blood" were in reality diseases of the blood-forming organs. The blood cells, after all, do not inhabit the blood, but come into it from widely-scattered centers of active, cellular growth. Many factors influence these centers. Thus, who could have foretold ten years ago the striking relationship between the bone-marrow

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and the stomach which Castle so beautifully demonstrated in 1929? There are but few diseases which fail to influence in some measure the blood-forming organs. By observation of the peripheral blood it has thus become possible not only to gain insight into the workings of various infectious processes, but to deduce what is happening at a given moment in the bone-marrow or the lymphoid tissue. In other words, emphasis has shifted from a purely morphological "peripheral" study of the blood cells to a comprehension of the underlying physiological and pathological principles. With this shifting of emphasis has come a shift in the geographical center of hematological study from Europe to this country. American investigators, by adapting physiological principles to the "blood" diseases have made such striking advances in their therapy that the center for hematology has been completely taken from Europe to this country.

Survey of the Literature

I. The Blood-Forming Organs

The cells which circulate in the blood arise from three widely-scattered centers of active cellular growth which have come to be called "organs". These are the bone-marrow, the lymphoid tissue, and the reticulo-endothelial system.

A. *The Bone-Marrow.* The article of Florence R. Sabin written in 1928 is a classic and repays careful reading. Active red marrow is scattered throughout the flat bones, and in the vertebrae and the epiphyseal ends of the long bones. Here all of the red blood cells, all of the blood platelets, and about 70 per cent of the white blood cells are formed. There is a growing interest in the study of this important organ as a means for the better understanding of blood pictures. Pathologists, content in the past to note the gross appearance of the marrow at the head of the femur, have turned their attention to the microscopic study of marrow tissue. Custer[1] has done a great service in standardizing bone-marrow findings from autopsy observations. Much more is to be learned, however, from sections of the marrow removed at biopsy. Impetus to this study was given by Seyfarth (1923) who devised a trephine for removal of marrow from the easily accessible sternum. Since then several studies have appeared and various modifications of this trephine have been made (Arinkin, Arjeff, Tuschinsky and Kotlarenko, Custer[2], Dameshek[1]).

Correlation of the findings in the bone-marrow with those in the peripheral blood has resulted in greater knowledge regarding the underlying pathological physiology of pernicious anemia (Tempka and Braun) and primary hypochromic anemia (Dameshek[2]) and has resulted in greater diagnostic acumen with regard to obscure blood pictures due to aleukemic leukemia (Dameshek).

B. *The Lymphoid Tissue.* Lymphocytes are formed in various lymphoid structures: the lymph-nodes, spleen, tonsils, Peyer's patches of the intestine. They are derived from lymphoblasts which are in turn probably derived from even more primitive cells in the germinal centers of the lymph-nodes (histiocytes?—reticulo-endothelial cells). It is possible that both in the spleen and lymph-nodes, two distinct lines of cells are developed: lymphocytes and monocytes, both arising originally from the primitive mesenchymal cell: the histiocyte.

C. *The Reticulo-Endothelial System.* No field in hematology has commanded greater attention in recent years than that of the reticulo-endothelial system. Until recently, much controversy took place regarding even the acceptance of such a "system". However, in the last few years, so much evidence has accumulated regarding the histology, physiology, chemistry, pathology, and reactions of this group of cells that but few remain to combat the concepts so well enunciated by Aschoff and Kiyono.

The reticulo-endothelial "system" is the sum-total of a large number of cells which are gathered principally in the spleen, lymph-nodes, liver and bone-marrow, but are also present in the omentum, the skin, etc. The reticular cells of the spleen, the reticular cells of the lymph-nodes, the Kupffer or stellate cells lining the endothelial spaces of the liver, and the reticular cells of the bone-marrow are all constituent parts of this system (Aschoff and Kiyono; Maximow; Schittenhelm; Krumbhaar; Bloom; also see Dameshek[1, 2]). These reticulo-endothelial cells are large, of irregular shape (usually spindle-shaped); the nucleus is spongy and "basket shaped". They are actively phagocytic and rapidly engulf injected particles (neutral red. carbon, thorium dioxide) (Radt); they produce bile (bilirubin) from broken-down red blood cells (Haldeman); they store fat (cholesterol, kerasin) (Epstein); they are actively concerned in foreign-body reactions and tend to form giant cells; they are probably concerned in certain immunological processes (Schittenhelm); they produce the third type of white blood cell: the monocyte (quoted by Dameshek[2]). They are probably the direct representatives in the adult human of the primitive mesenchyme (Maximow).

II. The Blood Cells

A. *Derivation.* Some note should be made in this review of the present status of the derivation of the blood cells. (For good discussion see Piney and Maximow, also Doan.) There can be no question that the blood cells in general are neither epithelial nor entodermal structures, but are mesenchymal in origin. The unitarian or monophyletic school maintains that the primitive mesenchymal cell, the hemohistioblast, the histiocyte, still functions in the adult to produce all types of blood cells. The dualists claim

that the primitive stem-cell is lacking but that there is (1) a bone-marrow or myeloid stem producing the red cells, the platelets, the granulocytes, and the monocytes and (2) a lymphoid stem producing lymphocytes. This view is held chiefly by Naegeli and finds but few other supporters. The trialists claim that only the secondary stems are present in the adult: myeloid, lymphoid, and reticulo-endothelial. There is but little actual difference between the monophyletic and trialistic schools, but it seems to the reviewer that the trialistic view, originally championed by Schilling, is at present in the ascendancy. According to this view, the monocyte is derived directly from the system of histiocytes, the reticulo-endothelial system, and is distinct from either the myeloid or the lymphoid cells. The evidence for this view is cited by Dameshek.

B. *Terminology.* The terminology for the description of the red blood cells and blood platelets remains but little affected. The white blood cells, however, have suffered some changes in terminology. In the interest of simplification and the avoidance of controversial terms, the word *monocyte* has come into general use and the terms "large mononuclear cell," "transitional cell," and "endothelial leukocyte" have been in great part discarded in hematological literature (see description of monocyte). The term "large mononuclear cell" comprised both the large lymphocyte and monocyte and has been productive of much confusion. The concept of Ehrlich that the monocyte represents a transition between a myeloid and a lymphoid cell has been proved incorrect. Mallory's term "endothelial leukocyte" presupposes derivation of the monocyte from endothelial surfaces; this view does not hold general acceptance.

The popularization of the Schilling index (q.v.) has introduced several new terms into English hematological literature. The simplest translations for the German words "bandform", "stabkernigform" and "jugendform" are "band form", "staff form" and "young form". Schilling's book on the "blood picture" was literally translated into not very idiomatic English by Gradwohl and the latter author is to be credited with the introduction of such terms as "stab cell" and "juvenile cell" (band form and young form of polymorphonuclear). Modifications of Schilling's hemogram in this country are given below.

C. *The Schilling Index and Hemogram.* Arneth devised a classification or index of the maturity of the polymorphonuclear cells based upon the number and shape of the nuclear lobes. Although this index was undoubtedly useful in the determination of the degree of severity of an infectious state, it proved too cumbersome for general use and was gradually discarded. Schilling began writing of his simplified index of the types of polymorphonuclear cells in 1911. By 1925, his method for making differential counts of the white blood cells was in general use in Germany and in most continental countries. It is only in the last few years that the method has come into fairly wide use in this country. (See Piney for good discussion.)

In order to understand this index, it is necessary to study the maturation of the polymorphonuclear cells in the bone-marrow. The most primitive polymorphonuclear cell, the myeloblast, need not concern us here. The *myelocyte* is characterized by a round nucleus and many coarse granules scattered over the nucleus and cytoplasm. As this cell matures, there is at first slight indentation of the nucleus, the *young form* of metamyelocyte, to be followed by more marked indentation, the *band* form of metamyelocyte. The nuclei of both the young and band forms are characterized by smooth outlines. The nucleus of the band form gradually becomes concentrated into lobes: the mature polymorphonuclear cell. These types of polymorphonuclear cells may be conceived as occupying layers in the bone-marrow. Farthest away from the circulation are the myelocytes, nearest are the mature polymorphonuclear cells. By the natural expansion of the growth process, the mature polymorphonuclear cells are pushed into or by ameboid activity get into the circulation. Most infectious processes are accompanied by a need for polymorphonuclear cells. The stock of mature polymorphonuclear cells is quickly exhausted, and (as in war), younger cells are drafted. First come the band forms, then the young forms, finally myelocytes and possibly even myeloblasts. By observing the peripheral blood during an infectious process, one can gauge the severity of an infection and frequently its outlook. The differential count by this method (Schilling hemogram), is made by counting 100-200 white blood cells (preferably the latter number). Each cell is classified as in the ordinary differential count, except that the polymorphonuclear cells are divided into the types outlined above. The total polymorphonuclear count as well as the percentages of the various types of polymorphonuclear cells are recorded in some such form as this:

Polymorphs.	Eosinophiles	Basophiles
Mature		
Band		
Young		
Myelocytes		
Lymphocytes		
Monocytes		

A "shift to the left" (toward the more "radical" or "young" form of polymorphonuclear cell), is seen when there is an increase in band

and young forms over normal and is an accompaniment of all infectious states even when leukopenia is present. Normally, less than four per cent of band forms are present. A mild infection brings about an increase of band and young forms (immature polymorphonuclear cells), to 15-20 per cent, a moderately severe infection to 20-40 per cent and a severe infectious state (septicemia, etc.) to 40-80 per cent. With subsidence of active infection, the following changes successively take place: (1) the appearance of an eosinophile or two; (2) a diminution in band forms; (3) an increase in monocytes, often to 15-30 per cent ("monocytic stage of defence"); (4) lymphocytosis. A marked lymphocytosis of 40 per cent or more is commonly seen and is usually accompanied by an eosinophilia of 4-10 per cent. This is the last or "healing" stage.

Several modifications of the Schilling method have been practised: the filament or non-filament count (Farley, St. Clair, and Reisinger), the Cooke index (Cooke and Ponder). They are all similar, and it becomes a matter of taste which index one uses. It must not be supposed that these methods of making a differential count of the white blood cells represent short cuts for the formulation of a clinical diagnosis. By adding another feature to the mosaic which, in its entirety, represents a diagnosis, they are however of distinct value.

D. *The Monocyte, the Histiocyte, Supravital Studies.* The *monocyte* has become the most widely discussed of the blood cells. There are two reasons for this: (1) it is in all probability the direct representative in normal, circulating blood of the reticulo-endothelial system which has loomed so large in recent years; (2) by its separation as a cell distinct from both the myeloid and the lymphocytic series, its importance in the differential count of the white blood cells has become distinctly greater and therefore a matter worthy of careful study.

The cell is easily recognized if various characteristics of cytoplasm and nucleus are kept in mind. It is the largest normal cell of the circulating blood, 12-20 micra in size, oval in shape, frequently irregular in outline with "pseudopods" jutting off from its borders. The cytoplasm is stained grayish-blue with Wright's stain and contains innumerable very small violet granules. The nucleus fills about 0.7 of the cell, is usually indented and bean-shaped in outline and is made up of fine chromatin network.

Supravital investigations popularized by Sabin have shown that the cell is actively motile through the formation of pseudopods, and gathers neutral red granules in the bend of the nucleus. Much has been written in recent years of the supravital method for studying the white blood cells. (Cunningham and Tompkins[1].) Some authors have claimed that only by this method is it possible to distinguish clearly the monocyte from the large lymphocyte and thus perform a careful differential count in certain diseases in which the percentage of monocytes may be of value. (Blackfan and Diamond; Hertz and Lerman.) It is the reviewer's opinion that the importance of supravital study of the blood cells has been overemphasized. It is possible, by careful study of the stained blood smear, to differentiate clearly the large lymphocyte and the monocyte. The supravital method is not without its own intrinsic errors, not to speak of the difficulty attending its use in ordinary clinical practice. (Tompkins; Hall.) The writer has found it to be of limited value, particularly in the study of the frequently atypical cells of acute leukemia, in the differentiation of the monocyte and the abnormal lymphocytes in "infectious mononucleosis" (at times a difficult matter) and in the study of certain aspects of the physiology of the white blood cells.

The *monocyte-lymphocyte ratio* (M:L ratio) has been made much of since Cunningham, Sabin et al demonstrated that in active tuberculosis of experimental animals, the monocyte was the important type-cell of the infection and became much increased at the expense of the lymphocyte. With development of the disease, these investigators found that the ratio of monocytes to lymphocytes, normally about 0.3 to 1, became frequently 1 to 1 or higher. Cunningham, Sabin, Sugiyama, and Kindwall and Cunningham and Tompkins[2] studied the M:L ratio in clinical tuberculosis and found it to be of value in the prognosis and follow-up of the disease. Many investigations were made of its clinical value and were followed by enthusiastic reports, which have however not been fully sustained. It is true that the monocytes become increased in tuberculosis and that at times, the M:L ratio is greater than 1. This may hold true much more for infants (anergic individuals) than for adults in whom allergy and superimposed infections complicate the picture. Various investigators have pointed out that the Schilling hemogram gives much more information than does the calculation of the M:L ratio.

Again, monocytosis accompanies most subacute infections (sinusitis, general paresis, subacute bacterial endocarditis), the M:L ratio frequently becoming increased. The normal monocyte count is 8-12 per cent of the total white blood cells and becomes increased, not only in subacute infections but in typhoid fever, chronic sepsis, agranulocytosis, hyperthyroidism and Hodgkin's disease. With marked increase in monocytes, it is usual to find an occasional histiocyte. (Dameshek.)

The *histiocyte* is never seen normally, but only in those conditions in which a monocytosis is present (i.e., in overactivity of the reticulo-endothelial system). It is extremely large, ex-

tremely irregular in shape, usually with pseudopods. The cytoplasm is sky-blue in color, frequently contains phagocytosed material and vacuoles. The granules are large, azure and grouped about the nucleus. The latter is typically "spongy" with a loose chromatin mesh and a thick perinuclear membrane. Supravitally, this cell is distinguished by its rapid motility and its phagocytic tendencies. Its appearance in the circulation has been emphasized in subacute bacterial endocarditis, but the reviewer has demonstrated its frequent presence in other conditions. (Dameshek.)

E. *The Blood Platelets.* Many methods for the enumeration of the blood platelets have appeared in the last few years. Several of these have emphasized the inaccuracy of the platelet counts and the probably low figure ordinarily given for the blood platelet count (about 200,000 per cu. mm.) (Olef.) The reviewer by studying a large series of normal men and women found that the normal range of count in men is 600,000 to 900,000 but that in women the count is complicated by the menstrual cycle. With menstruation, there is an extreme rise in the platelet count, between periods the count being relatively low. The "direct" method for counting blood platelets is probably grossly inaccurate, indirect counting by studying under oil immersion the relation of the blood platelets to 1000 red blood cells being of much greater accuracy. A few authors have recently touched upon the changes in the morphology of the platelets which may occur in various conditions. (Pepper and Farley; Mackay.) Study of the platelets becomes important, not only in the hemorrhagic diseases, but in the estimation of the function of the bone-marrow. With the white blood cell count, the number of polymorphonuclear cells, and the percentage of reticulocytes, enumeration of the platelets gives a complete index of bone-marrow activity.

F. *The Red Blood Cells.* These cells, peculiar in their absence of a nucleus and in their remarkable affinity for oxygen and carbon-dioxide, have been shown to be intimately concerned with gastric digestion which apparently elaborates a specific growth producing hormone (*stroma-building substance,* "addisin"). (See Castle and Morris et al under "The Macrocytic Anemias.") Without this substance, the marrow red blood cells do not maturate, and an embryonic (megaloblastic) type of red blood cell formation takes place with resultant macrocytic (pernicious), anemia. Stroma may be built up in the absence of iron-containing foods, but the red blood cells in an iron-deficiency state become achromic, there is a low "color" index, and obviously their oxygen-carrying efficiency or capacity becomes impaired.

The stage before the formation of the completely adult red blood cells is the *reticulocyte,* which, when stained supravitally, shows a distinct network. The reticulocyte has become the indispensable tool for investigations regarding the efficacy of various substances used in the treatment of pernicious anemia. Although not generally known, it is also valuable in estimating the response in the hypochromic ("secondary"), anemias to iron and other therapy. (Keefer and Yang, Minot and Heath, Mettier and Minot, Dameshek.)

The great majority of mankind possesses round red blood cells. A few families, generally of the colored race, possess cells which are longer in one diameter than in the other. These are at times oval, at times elliptical, at times even "sickled". This disorder of the red blood cells, apparently an inherited characteristic, is not limited to the colored race, but may be seen in whites. (Literature well reviewed by Steinberg.) A Jewish family showing oval and elliptical cases was recently studied by the writer at the Beth Israel Hospital. Sickle-cell anemia appears to be the ultimate in this abnormality of the red blood cells.

Knowledge of the *blood-groups* has become all-important in the matter of blood-transfusion. Much confusion having arisen between the Moss and Jansky classifications, an international classification was devised in which the blood corpuscles are classified according to their content of agglutinin-forming substance (agglutinogens). Thus the four groups are

O (Type I Jansky; universal recipient; contains no agglutinogens)
A (Type II Jansky; contains agglutinogen A)
B (Type III Jansky; contains agglutinogen B)
AB (Type IV Jansky; *universal donor;* contains both agglutinogens)
(See Snyder)

The blood-groups are also utilized occasionally as a test for paternity. Wiener has shown that the chances for diagnosing paternity, which are about 1 to 6 using the above groups, are increased to 1 to 3 when the recently discovered groups M and N are utilized. For further details, the reader is referred to Wiener's articles.

The *sedimentation rate* of the red blood cells may be mentioned in passing. For careful investigations of this phenomenon, the reader is referred to the articles of Rourke and Ernstene. The sedimentation rate is chiefly useful in following along various chronic or subacute infectious states such as tuberculosis and rheumatic fever. If used as a routine measure in a large clinic, it may occasionally aid in establishing the presence of organic disease in a patient.

III. Disorders of the Blood-Forming Organs

A. *Associated Physiological Factors.* The bone-marrow, the lymph-nodes, and the reticulo-endothelial system have already been mentioned. The relationship of the stomach to red blood cell formation has been commented upon and

will be discussed in greater detail below. The intestines are also concerned because of their importance in the absorption of both stroma-building and hemoglobin-building material. With marked anemia, there are frequently lingual disorders (glossitis, atrophy of the tongue, etc.) and disorders of the central nervous system. Red cell destruction by the reticulo-endothelial system is a constant accompaniment of red cell formation and the chief product of this destruction is the non-iron containing yellow pigment bilirubin. With increased red blood cell destruction, there is an increase in the content of bilirubin in the blood (icterus).

The blood clots because of its content and quality of blood platelets. In hemophilia, although the platelets are normal in number, they are apparently deficient in quality, and the coagulation time is increased. In thrombocytopenic purpura, the platelets are diminished and although the blood clots in normal time, the bleeding time from small capillaries is much increased. In certain conditions, the red blood cells are more fragile to hypotonic salt solutions.

B. *Outline for Study of a Patient.*

History

Physical Examination: Particular reference to the following: *pallor*—("palm color" test very satisfactory—Duke); appearance of *tongue* (papillae, shiny appearance, coat, etc.); finger nails (see under Primary Hypochromic Anemia); hair (see under Pernicious Anemia and Primary Hypochromic Anemia); lymph-nodes; size of spleen (percussion and palpation); sclerae of eyes for icterus; reflexes; vibratory sensation of the extremities with tuning fork; skin for ecchymoses and petechiae.

Laboratory Tests

Routine: Hemoglobin (Tallqvist worthless; Sahli if calibrated with Van Slyke-Neill oxygen capacity, good*; Dare poor). R.B.C. W.B.C. Blood Smear: differential count of the white blood cells with use of the Schilling hemogram, examination of the red blood cells for achromia, aniso- and poikilocytosis and polychromatophilia; blood platelets.

Anemia: Blood platelet count; reticulocyte count; icterus index; quantitative bilirubin (Van den Bergh); measurement of the red blood cell diameter (micrometer eyepiece—Price-Jones); Hematocrit and determination of the various indices (volume index, mean corpuscular volume most valuable). (Haden, Wintrobe.) Gastric analysis with histamine. (Bloomfield and Polland.) Stool for occult blood. Bone-marrow biopsy in the rare difficult case. Fragility test in the anemias with jaundice.

*Leitz apparatus has been found satisfactory. Tendency in recent years has been to estimate hemoglobin in Grams per 100 cc. of blood. 100% is 17.2 grams by Sahli; 16.2 grams by Newcomer, 14.5 grams by Dare, etc. See articles of Osgood and Haskins.

Leukemia: As above. Oxidase test (Sato-Sekiya); supravital studies;? bone-marrow biopsy.

Hemorrhagic Diseases: Bleeding time. Clotting time. Clot retraction. Tourniquet test.

Lymph-node Enlargements: Blood studies as above. X-ray chest. X-ray long bones. Bence-Jones protein in urine. Biopsy of a lymph-node. ? Basal metabolism test.

C. *Bone-Marrow Disorders*

1. *The Red Blood Cells*

(a) *The Anemias*

(aa) *Classification.* There are various methods for classifying the anemias. Some of the more simple classifications are not inclusive and some of the more complex classifications become confusing. Primary, idiopathic, or essential anemias are contrasted with those secondary to known cause. In recent years it has seemed wise to classify red blood cell disorders on the basis of hemoglobin content: thus "macrocytic" refers to the anemias with large cell size and high color index and "hypochromic" to those with low color index, achromia, and small cell size. Among the macrocytic anemias (and those other anemias in which there is a deficiency in stroma-building substances) are pernicious anemia, and among the hypochromic anemias one finds not only primary hypochromic anemia but secondary anemias as well. Until the exact etiology of the anemias is known, it seems best to adopt these morphological criteria. Attempts have been made to classify the anemias on their pathological aspects. Thus, pernicious anemia is megaloblastic anemia; the name aplastic anemia is satisfactory; primary hypochromic anemia is erythronormoblastic anemia; congenital hemolytic jaundice is hyperreticulosis. (Dameshek.) This may become the method of choice if the pathological picture of each disease becomes well-established. Other methods of classification which may be mentioned are those referring to blood and cell volume. (Wintrobe; Haden, Osgood.) For a good general discussion of the anemias see Witts. The most recent simple classification which I have used is the following:

a. *Macrocytic*—large cells, high color index, high mean corpuscular volume. Includes pernicious anemia and associated conditions.

b. *Hypochromic*—small cells, low color index, low mean corpuscular volume. Includes "primary" hypochromic anemia and the anemias secondary to known cause (hemorrhage, sepsis, malignancy, etc.).

c. *Aplastic*—no growth of the marrow, resulting in marked diminution in red blood cells, white blood cells, and blood platelets.

d. *Myelophthisic*—invasion of bone-marrow by malignant or leukemic processes. Anemia, leukopenia and thrombocytopenia result with evidences of attempted regeneration.

e. *Hemolytic*—increased destruction of red blood cells through overactivity of reticulo-endothelial system or by other cause. Includes congenital and acquired types.

(bb) *The Macrocytic Anemias.* The name of William B. Castle stands out brilliantly as the great investigator of those conditions characterized by anemia with large cell size and high color index. As the direct result of his investigations has come an entirely new conception of pernicious anemia as a conditioned deficiency disease dependent upon a gastric mucosa which is incapable of carrying out the first stage of protein digestion and thus nourishing the bone-marrow with the specific product apparently necessary for normal red blood cell growth. (Castle *et al*[1, 2, 3].) As by-products have come the discoveries of the potency of gastric mucosa ("ventriculin") (Sturgis and Isaacs) and of concentrated gastric juice intramuscularly injected. (Morris, Schiff, Burger, and Sherman.)

Castle showed first that beefsteak given alone to patients with pernicious anemia was ineffective but that beefsteak when incubated with normal gastric juice produced as typical a reticulocyte and red blood cell response as though liver extract had been given. The gastric juice of the patient with pernicious anemia was evidently deficient in a substance ("x" factor) which was present in the normal gastric juice. Thus, protein could be eaten *ad libitum* by the patient with pernicious anemia but was without effect on the bone-marrow, i.e., a deficiency existed although sufficient material was ingested. This was a "conditioned" deficiency. Attempts to isolate in pure form this "x" substance have been unsuccessful although some of its characteristics are known, i.e., that it is probably an enzyme of organic nature, thermolabile, and active in neutral solution. Cheney and Niemand have attempted to show that the possible enzyme is trypsin.

In further logically-drawn experiments, Castle *et al* showed that pernicious anemia was a disease dependent upon the lack of interaction between an "extrinsic" factor (in the food) and an "intrinsic" factor in the gastric juice. It would therefore be possible theoretically to produce pernicious anemia by the absence of the "extrinsic" factor, even though the intrinsic factor was present. This reasoning led to Castle's brilliant investigations carried out with Rhoads in Porto Rico which showed that sprue was in reality pernicious anemia (Castle and Rhoads). In certain cases of sprue, the gastric juice contained the "x" factor but the dietary was so deficient in the extrinsic factor that a macrocytic anemia developed. The concept that pernicious anemia was only one of several macrocytic anemias was gradually built up. Thus macrocytic anemia could develop (1) *in the absence of the extrinsic factor* (poor dietary, sprue, certain cases of pellagra) (2) in the complete absence of the intrinsic factor, (pernicious anemia) or during its temporary suppression (pernicious anemia of pregnancy, Strauss and Castle[1]) (3) in severe diarrheas (ulcerative colitis—pancreatic disease—coeliac disease) in which although extrinsic and intrinsic factors were both present, there was deficient absorption by the intestine of the end-products of gastric digestion. Further experiments with the extrinsic factor by Strauss and Castle[2] demonstrated that not only beef but various other proteins were active. The final demonstrations led to the highly interesting discovery that vitamin B_2 was the simplest and most active extrinsic substance. At the present writing it would appear that the macrocytic anemias are vitamin deficiency diseases dependent upon the failure of the bone-marrow to receive either sufficient vitamin B_2 or a substance derived from this vitamin. This theory, built up so logically by Castle and his collaborators was recently jolted by the publication of the results of Morris *et al,* who gave intramuscular injections of highly concentrated gastric juice to patients with pernicious anemia and produced striking response. Morris and his collaborators feel that the normal gastric juice contains a hormone (which they call "addisin") necessary for the normal functioning of the marrow. This hormone is apparently effective even in the absence of Castle's extrinsic factor. Further studies are necessary before these results can be completely accepted.

The treatment of pernicious anemia has become bewildering. Almost weekly, the clinician is regaled with some new product. Liver extract, gastric extract, combinations of liver extract with gastric extract (Fouts and Zerfas), liquid liver extracts of various types, and recently numerous preparations for intramuscular injection have been introduced. There seems to be a definite trend away from the liver extract in powder form for oral use toward intramuscular products which are given by the physician at weekly or longer intervals. Numerous intramuscular products of various degrees of concentration have been placed on the market (Strauss, Taylor and Castle; Murphy; Richter, Meyer and Ivy). It is possible that some of these products have been inadequately assayed and that the potency of some is much greater than that of others. It is not yet known whether the material derived from 10 Gm. of liver given intramuscularly represents a maximal quantity or whether it is necessary in a given case to administer doses of extract derived from 100 Gm. of liver. All authorities are agreed that in those cases of pernicious anemia showing central nervous system lesions, maximal, frequently repeated doses are necessary to obtain beneficial results.

Cases of "combined system disease" are becoming recognized much more frequently. Often they are associated with what at first glance is

an almost normal blood picture. However, careful investigation will usually show the following: slight reduction in red blood cells (3.5-4.0 million), high color and volume index, increased mean corpuscular volume, low white blood cell count, macrocytes, presence of "pernicious anemia-neutrophiles", slight diminution in blood platelets, slight increase in icterus index, complete achlorhydria. At times, no blood changes can be recognized or there is even a hypochromic picture. The full-blown case is characterized clinically by spasticity, increased knee and ankle-jerks, positive Babinski response, and absent vibratory sensation. However, all gradations exist between this type of case and that showing only paresthesias of the extremities with diminished vibratory sensation together with glossitis and achlorhydria. It is becoming more and more evident that prolonged intensive treatment with intramuscular liver extracts will benefit the great majority of these cases, even those which appear hopeless (Greenfield and O'Flynn; Baker). The mild ones may expect complete recovery, and even those with extreme spasticity and signs of degeneration of the posterior columns frequently become strikingly improved. It is probable that the best results are obtained from frequently repeated injections of concentrated extracts of liver.

Cases of macrocytic anemia not idiopathic in type but associated with pregnancy, fish tapeworm (Birkeland), tuberculosis, syphilis, sprue, poor dietary, etc., are treated in identical fashion with pernicious anemia and with as good results, despite the presence of these other factors. Attempts should be made, however, to clear up associated conditions.

(cc) *Hypochromic Anemias.*

One of the most interesting of recent developments in hematology has been the exclusion from the large ill-defined category called "secondary anemia" of a group of cases which has been called "primary or idiopathic hypochromic anemia". In these cases, although the blood-picture is that of "secondary anemia", (low color index, achromia of the red blood cells) no apparent cause for this abnormal blood picture can be demonstrated. Kaznelson, Reimann and Weiner, Davies, Witts, Haden, Wintrobe and Beebe, Dameshek and others have shown that the disease is almost wholly confined to women, usually in middle life, who complain of weakness, lassitude, burning tongue, paresthesias, gastro-intestinal disturbances, and brittle finger-nails. Examination discloses "white" pallor, usually grey hair, an atrophic tongue which is usually distinctly reddened and devoid of coat and papillae, and frequently flattened, hollow finger-nails. The hemoglobin is depressed to a far greater degree than is the red blood cell count (ordinary findings are hemoglobin 40%, red blood cell count 3.5 million); the color index is very low, the white blood cell count is low, 3000-6000, the blood platelets are somewhat reduced, the polymorphonuclears are usually reduced and the red blood cells show marked achromia and are smaller than normal in average size (microcytosis). In almost every case, gastric analysis reveals complete achlorhydria even after stimulation with histamine. Dameshek[1] showed that the bone-marrow, despite the anemia, is crowded with nucleated red blood cells of the normal type (erythroblasts, normoblasts). A striking feature is the dramatic response to large doses of iron which result in definite reticulocyte response, a rapid rise in hemoglobin, increased appetite, gain in weight, and subsidence of all the symptoms. There is tendency to relapse, however, when medication is discontinued.

The many features which this disease presents in common with pernicious anemia have been the subject of much comment and it is doubtless true that the disease is just as "primary" as pernicious anemia. Davies, Wintrobe and Beebe; Kaznelson, Reimann and Weiner; and the reviewer, suggested that a gastric defect is present interfering with the normal digestion of iron-containing foods and resulting in an iron deficiency. An experiment along the lines of Castle's work with pernicious anemia was done by Dameshek[2] with suggestive results.

Most cases are completely idiopathic, but some are associated with menstrual bleeding (which often diminishes when the anemia improves), some with pregnancy, myxedema, tape-worm, or dysphagia (Plummer-Vinson syndrome). The factor common to these cases seems to be a gastric defect which is shown clinically as achlorhydria. Individuals with this defect appear to be more vulnerable to the development of anemia so that when a factor such as poor dietary, pregnancy, etc., appears, anemia of the hypochromic type is very likely to occur.

The disease, which appears to be an actual deficiency in iron (Heath, Strauss, and Castle; Alt) is treated by the use of large doses of iron. Minot, Heath, Dameshek[3] and others have demonstrated that at least 1000 mgs. of available iron are necessary for maximal results in most cases. To obtain this, the following daily dosages of the various iron compounds are necessary:

Ferric ammonium citrate	6 Gm.
Reduced iron	3-6 Gm.
Blaud's pills	20 pills
Ferrous chloride	2.0 Gm.
Ferrous glutamate	6 Gm.

Certain cases need larger doses of iron. When tremendous doses of iron cause no further rise in hemoglobin, copper may be tried. The reviewer has noted that when the hemoglobin percentage becomes "fixed" during iron treat-

ment, small doses of copper sulphate (0.005 Gm. daily) given together with large doses of iron, almost always cause resumption of hemoglobin rise.

Most authorities agree that liver is of no value in these cases, although Murphy concludes that intramuscular liver, given as an adjunct to iron therapy, is of distinct value. The various proprietary "shot-gun" mixtures which contain iron, liver, hemoglobin, copper, etc., are much more expensive and of no greater value than their contained iron. The exact place of copper in the treatment of this type of anemia in man has still to be settled, although it has several protagonists.

(dd) *Secondary Anemias.* These are treated in much the same way as the above, but with the added responsibility of dealing with the cause. In the presence of infection or malignancy but little headway can be made against anemia. The same holds true with chronic nephritis in which the prognosis can often be gauged by the extent of the anemia.

(ee) *Aplastic Anemia.* In the past the great majority of cases of aplastic anemia (striking anemia, leukopenia, thrombocytopenia) were thought to be primary or idiopathic in type, but in recent years so many substances have become incriminated as the cause of bone-marrow aplasia that it behooves the physician to search for a cause in each case diagnosed as aplastic anemia. Arsenic, arsphenamine, x-rays, radioactive materials, benzol and silver have been shown to cause destruction of bone-marrow tissue, usually total, at times selective. If selective, only anemia or leukopenia or thrombocytopenia may develop. Very recently gold (sanocrysin, gold sodium thiosulphate) has been found to cause various bone-marrow disorders and the writer has observed a typical case of aplastic anemia following its use in the treatment of lupus erythematosus.

The treatment of aplastic anemia is the use of repeated transfusions of blood until the patient either shows signs of recovery or until proof is presented that no evidence of bone-marrow regeneration exists. Recently pentnucleotides (see under Agranulocytosis) have been used with possibly successful results in a few chronic cases. Some observers recommend splenectomy which is supposed to remove an organ inhibitory to the marrow.

(ff) *Anemias of Children.* These differ but little from those of adults except that changes may progress more rapidly, response may be more marked, evidences of immaturity of cells may be more striking. However, in the last few years, two types of anemia occurring only in children have been stressed. These are (Cooley's) erythroblastic anemia and erythroblastosis of the new-born. Cooley's anemia is present chiefly among children of Mediterranean origin (Italians, Portuguese, etc.) and is characterized by marked splenomegaly, striking anemia with the presence of large numbers of immature nucleated red blood cells (erythroblasts) in the circulating blood. (Kato and Downey.) At times, cranial defects with the presence of striae by x-ray are present. Splenectomy is at times of curative value.

Erythroblastosis of the new-born is characterized by intense jaundice, edema, and striking anemia, the peripheral blood containing all of the elements ordinarily seen only in the bone-marrow: myeloblasts, myelocytes, megaloblasts, erythroblasts, bits of megakaryocytes, etc. Pathologically, Ferguson and others have shown that the outstanding feature is the occurrence of abnormal extramedullary hematopoietic activity of an embryonic type ("megaloblastic, hemohistioblastic, erythroblastic" according to the author). The jaundice is apparently due to "excessive hemolysis of large numbers of imperfectly differentiated erythrocytes loading the liver cells with bile pigment more rapidly than it could be taken care of by the bile-excreting apparatus" (Ferguson). The edema is probably due to hypoproteinemia and is related to the previously described hydrops of the new-born.

An interesting condition apparently more common in infants than in older children and possibly congenital in nature is aplastic anemia (Morquio and Volpe).

(b) *Polycythemia Vera.* The production of red blood cells in the bone-marrow is tremendously increased in this condition, the erythrocyte count often reaching ten to twelve million. Some observers have contended that the erythrocytosis is neoplastic in type, but it is probable that the disorder is frequently constitutional or hereditary and begins early in life. It usually goes unrecognized (except in medical students doing red counts) until the patient presents himself with heart disease, arteriosclerotic manifestations including thrombosis, or hemiplegia. The importance of arteriosclerotic disorders in this disease cannot be overemphasized (Brown and Griffin). The spleen is enlarged in almost every case, except possibly in the special (?) type associated with hypertension (Gaisböck). Morris has recently advanced the interesting suggestion that the underlying cause is intense bone-marrow stimulation from overproduction of "addisin" (see under Pernicious Anemia) in the gastric juice. He advises, therefore, the daily removal of gastric juice. Forkner has recently stressed the use of large doses of Fowler's solution which will reduce not only the red cell count but also the high white blood cell count and the blood platelets. Numerous observers stress the value

of radiotherapy as a means of reducing cellular growth in the marrow. Phenylhydrazine hydrochloride continues, however, to hold a leading place in treatment in dosages of 0.030 to .240 daily, dependent upon the individual involved. Frequent counts of the red and white blood cells and observation of the patient for icterus are necessary during this form of therapy. When the red cell count remains fixed at 5.0 million or thereabouts, a maintenance dose of about 120 to 150 mgs. weekly is usually effective. Recently acetylphenylhydrazine has been reintroduced. The warning must be given that it is necessary to treat not only the red blood cells but the patient as well. Some patients have been irremediably damaged by too strenuous efforts to treat the red blood cells rather than the patient.

2. *White Blood Cells*

(a) *Agranulocytosis.* Since publication of the last report on progress in hematology, a new disorder has been generally recognized, widely reported from over the entire world, classed as almost always fatal, and finally to a great extent conquered. Reported as agranulocytic angina by W. Schultz in 1922 because of the severe throat lesions associated with lack of granulocytes in the peripheral blood, the name was gradually modified to agranulocytosis because of the many cases reported in which angina was absent. To some the word agranulocytosis is objectionable and such terms as malignant neutropenia, primary granulopenia, primary granulocytopenia have been proposed (excellent review of the subject by Beck). Although granulocytes may disappear from the peripheral blood in the course of severe infectious states, it has gradually become manifest that agranulocytosis does not represent an infection but is a primary bone-marrow disorder in which the white blood cell forming mechanism becomes depressed (Beck; Roberts and Kracke; Doan). The cause for this phenomenon is not known, but gradually, as the supply of the white blood cells in the peripheral blood becomes depleted, the patient begins to feel weak, depressed, and finally develops various lesions of mucous membranes (Roberts and Kracke, Doan, Dameshek). These in all probability are the result of unrestrained bacterial growth in the absence of granulocytes. The fully-developed clinical picture has been well described by many observers. At first, the disease was considered universally fatal, but occasional instances of spontaneous recovery were later noted. These were associated with a marked degree of monocytosis, indicating possibly that the reticulo-endothelial system was assuming some of the burden (Dameshek and Ingall). In 1930, Reznikoff used the nucleic acid derivatives adenine sulphate and guanine hydrochloride for raising the white blood cell count in cases of agranulocytosis. In 1932, Jackson et al introduced the "unbroken" pentose nucleotides (also derived from nucleic acid) which he and his co-workers used later in a large series of cases with excellent results. The mortality rate for agranulocytosis, 90 per cent before the advent of these measures, became quickly reduced to 10-20 per cent. Nucleic acid derivatives were for many years known to investigators as substances capable of raising the white blood cell count in animals. Their apparently specific results in cases of agranulocytosis, bringing about on the third to fifth day an increase in immature polymorphonuclears followed by an outpouring of more mature forms has been one of the most striking phenomena in present-day annals of therapeusis. The use of nucleotides in various infectious states attended with leukopenia has not been attended with much success. Some of the failures in the treatment with nucleotides are probably due to incorrect diagnosis, many physicians making the diagnosis of agranulocytosis merely because the white blood cell count is low, although the underlying condition may be (and frequently is) a leukemic process of the leukopenic or aleukemic variety or an aplastic anemia. Very recently liver extract has been injected intramuscularly with good results in a few cases. (Foran, Sheaff, and Trimmer.)

It must be remembered that in true agranulocytosis only the white blood cell forming elements are affected, the red blood cells and platelets being unaffected. As the cases of agranulocytosis have become pedigreed, their striking tendency to relapse has become well established as has the "neutropenic state" (Doan) with its accompanying weakness, fatigue, and depression.

(b) *Myelosis (Myelogenous Leukemia)*—see under "Leukemias"

3. *The Blood Platelets*

(a) *The Platelet Deficiencies and the Hemorrhagic Disorders.* The blood platelet count taken together with the reticulocyte count and the count of the polymorphonuclear cells offers a complete index of the function of the bone-marrow. The blood platelets are diminished when the bone-marrow is totally destroyed (aplastic anemia), when it is invaded by malignant disease (lymphosarcoma, leukemias) and in the disorder variously called thrombocytopenic purpura or purpura hemorrhagica. Blood escapes from capillaries when the blood platelet count reaches a "threshold level" which varies in individual cases, but is usually between 40,000 to 60,000 per cu. mm. This escape of blood from capillaries produces petechiae, usually first seen in the translucent mucous membranes, later in the skin. Larger hemorrhages produce ecchymoses. The cause of this marked deficiency in platelets when the rest of the bone-marrow is unaffected (white cell count and red cell count being normal or only slightly modified) is still unknown. Splenectomy is still being performed in the condition with good results. Transfusions

may be given with much success in tiding a patient over a relapse.

(b) *Non-Thrombocytopenic Purpuras.* Thrombocytopenic purpuras must be sharply differentiated from purpuric disorders, associated with normal blood platelet counts. Mention has been made that blood seeps out from the capillaries when the platelet count reaches a certain critical level. Leakage may also occur when the capillary wall is damaged although the blood platelet count is normal. Frank calls this condition "hemorrhagic capillary toxicosis". Schönlein's and Henoch's purpuras are probably of this type of disorder, as are the rheumatic purpuras, the infectious purpuras, those due to various chemicals such as arsenic, arsphenamine, phosphorus, gold, and to snake venom. The name "anaphylactoid purpura" has been applied by several writers (first used by Glanzmann) to this type of disorder, which in some ways is allied to urticaria, and occurs characteristically with serum sickness. The serum of horses immunized to increasing doses of snake venom ("anti-venin") has been used by some (Stockton and Franklin) in the treatment of this type of disorder with apparently good results.

(c) *Hemophilia.* In hemophilia the blood shows diminished tendency to clot. There is usually no spontaneous bleeding as in the purpuras, the bleeding following trauma and involving fairly large blood-vessels. Thus bleeding occurs following operations, fairly large cuts, trauma to joints, etc. Petechiae do not occur. This is probably due to lack of capillary involvement and to the normal blood platelet count. Recent investigators have adduced evidence which indicates that although the blood platelet count is normal, the platelets are qualitatively modified and do not clump together properly to form thrombi in response to trauma (Birch[1]). The occurrence of hemophilia in males, although the disease is transmitted by females, led Carol La Fleur Birch[2, 3] to suggest that males developed the disease because they did not possess ovarian hormone. Later, this investigator[2] differentiated hemophiliac males and non-hemophiliac males by determining that the latter had more "femaleness" than the former and thus did not bleed. She carried out her theories by treating hemophiliacs with ovarian substances. In one instance, she transplanted a normal ovary into the abdominal wall of a hemophiliac with apparently good results. A few reports of the apparently successful treatment of hemophilia with ovarian substance have served to confirm her work, which is still, to be sure, in the experimental stage. Brown and Albright have recently cast doubt upon the therapeutic effect of ovarian substance (estrin) in the disease.

(D) *The Leukemias.* As noted above, there are three types of white blood cells: (1) the granulocytes (2) the lymphocytes, and (3) the monocytes. These owe their origin in the blood stream to three separate sources: (1) the bone-marrow (2) the lymphoid tissue and (3) the reticulo-endothelial system. Leukemia might be better termed "leukosis" since it represents pathologically a generalized proliferation of the various types of white blood cells. This may be manifested by a high white blood cell count in the peripheral blood (leukemia) but may be associated with a normal or even low white blood cell count ("aleukemic leukemia"). Since there are three types of white blood cells and three separate blood-forming organs, three types of leukosis are possible. For many years, only myelogenous and lymphatic leukemias were thought to be present, but beginning with Schilling's publication in 1914 and culminating in recent years with a number of papers (Dameshek[1], Clough) the concept of monocytic leukemia as a third type of leukemia has become well established. This is characterized by proliferation of reticulo-endothelial cells throughout the body and, usually, by a tremendous number of mono- and histiocytes in the peripheral blood. An aleukemic form—aleukemic reticulosis (Dameshek[2]) is also described.

Leukoses may thus be myelogenous, lymphatic and monocytic. They may be associated with large numbers of circulating white blood cells or the white cell count may be diminished. Instead of the awkward term "aleukemic leukemia", it is probably better, as suggested by Piney, to use the terms "aleukemic myelosis", "lymphadenosis", and "reticulosis". Most observers feel that the leukoses are neoplastic proliferations of the various types of white blood cells, although Sternberg and others attack this view, particularly with reference to the acute leukoses, which, it must be admitted, resemble closely severe infectious processes.

Special reference should be made to the aleukemic leukoses. In an experience of about 100 cases of the various types of leukosis, the author has found that *the great majority are aleukemic.* These cases usually present themselves with anemia. In the aleukemic myelogenous type, splenomegaly is the outstanding feature. Because of this, Banti's disease or splenic anemia is frequently diagnosed, and pernicious anemia and secondary anemia are often considered. In the lymphatic type, generalized lymphadenopathy is almost always present. In the monocytic type, the lymph-nodes and the spleen are only slightly enlarged. All types are associated with moderate or severe anemia, leukopenia or a normal white blood cell count and thrombocytopenia. The anemia is frequently macrocytic in type and pernicious anemia is often diagnosed. Because the leukocyte count is low, agranulocytosis is considered. In the presence of ecchymoses and bleeding, the diagnosis of purpura hemorrhagica is frequently made. The reduction in red blood cells, white blood cells and in platelets suggests a "destructive" process of

the bone-marrow which is indeed borne out by bone-marrow biopsy. This shows marked cellular proliferation of various types with resultant crowding out of normal white blood cell, red cell, and megakaryocyte formation. In any case of obscure, long-standing anemia, the possibility of aleukemic leukosis should be considered. The chronic cases, particularly of the myelogenous type, are of long duration and in some cases splenectomy has been performed for relief of so-called Banti's disease.

The picture of aleukemic leukosis is given by various blood cell neoplasms which, by metastasizing into the bone-marrow produce anemia, leukopenia, and thombocytopenia. Thus lymphosarcoma may produce the picture of aleukemic lymphadenosis (lymphatic leukemia) with the appearance in the peripheral blood of abnormal lymphocytes and lymphoblasts. I have seen four such cases and two have been observed by Kato. Myelosarcoma (so-called chloroma, chloroleukosarcoma) may manifest itself terminally as aleukemic myelosis. In a remarkable case observed by Freeman and me recently (unpublished), a large uterine mass was removed and diagnosed ? sarcoma. Seven months later, I made the diagnosis of aleukemic myelosis which was confirmed by bone-marrow biopsy. At postmortem examination, in addition to the general "leukemic" process, several greenish tumors made up of oxidase positive cells were found. The uterine tumor was composed of oxidase positive myeloblasts. It is possible that reticulum-cell sarcoma may as a terminal event result in the blood-picture of monocytic leukemia. These combinations are further evidence that the leukoses are neoplastic processes of the white blood cells.

There has been no progress in the treatment of the leukoses, which as yet are universally fatal (Isaacs). Rare cases are reported in which although the course was consistently downhill, a remission of several months or more has occurred. Jackson, Parker and Robb report such a case and Gloor records one which was apparently cured following arsenic, x-ray treatment, thorium dioxide intravenously and transfusions of blood. Treatment with x-rays is of no value in the acute cases, except possibly in relieving slightly the distressing gingival lesions which are usually present, and the occasional generalized itching with or without manifest skin lesions. The chronic leukoses show definite relief in symptoms (itching, sweating, loss of weight, mediastinal symptoms, etc.) with radiotherapy (Isaacs). Forkner and Scott have recently reintroduced the use of large doses of Fowler's solution in the treatment of chronic myelosis. This is helpful in certain cases, particularly when radiotherapy cannot easily be obtained. Toxic symptoms frequently militate against its continued use.

E. *Disorders of the Lymph-Nodes.* The lymphoid cells are widely distributed throughout the body, although they are gathered in large groups in the lymph-nodes, the tonsils, Peyer's patches of the intestine, etc. Interspersed among these masses of closely packed lymphocytes are present large irregularly shaped cells with spongy nuclei; these are the reticular cells or the histiocytes of the lymphoid tissue (Maximow). It is possible that the forerunner of both the early lymphocyte and the reticular cell in the lymph-node is a more primitive, undifferentiated cell. However that may be, the lymph-node contains two different types of cells: the lymphoid cells and the reticular cells or histiocytes (Maximow). It is necessary to understand this clearly since a great deal of confusion has arisen when, in speaking of the proliferative disorders of the lymphoid tissue, they have frequently been indiscriminately grouped under the terms "lymphoma, lymphadenoma, malignant lymphoma," etc. Proliferative disorders of the lymph-nodes vary widely in nature and in type of cell even though they arise from the one organ. In general, it is possible to discriminate in a lymph-node between disorders of the lymphoid cells and those of the reticular cells.

1. *Disorders of the Lymphoid Cells*

Lymphoblast	localized	Lymphosarcoma
	generalized	Lymphatic Leukemia (acute) Aleukemic and Leukemic
Lymphocyte	local	Lymphoma
	general	Lymphatic Leukemia (chronic) Aleukemic and Leukemic
Plasma cell		Plasmacytoma "Myeloma"

A solid tumor made up of rapidly growing primitive lymphocytes (lymphoblasts) is called a lymphosarcoma. Originating anywhere in the body but principally in foci of lymphoid tissue as in the mediastinum, the tonsil, a Peyer's patch of the intestine, it rapidly grows into a solid mass and metastasizes widely into bone, bone-marrow, lung, etc. (Ewing). If it metastasizes into the bone-marrow, it gives the blood picture indistinguishable from aleukemic lymphatic leukemia (Kato).

A generalized proliferation of the lymphoblasts is called acute lymphatic leukemia. A solid tumor of more mature lymphocytes, relatively benign, is called lymphoma (lymphadenoma) in the strict sense; generalized, it is chronic lymphatic leukemia. Various gradations between the rapidly growing proliferative process made up almost entirely of lymphoblasts and that composed of the well-differentiated small lymphocytes are seen (Ewing).

A proliferative disorder of lymphocytes benign in type and probably infectious in origin has been called "infectious mononucleosis". This term is unfortunate for several reasons. In the first place, the cells are typically lymphocytes of various stages of maturity and not monocytes. As noted above, the term "large mononuclear cell" has to a great extent been discarded and replaced by the more precise terms: large lymphocyte and monocyte. Longcope was not certain of the exact type of cell concerned in the blood-picture of what had until his studies been called "glandular fever" and so used the indefinite name "infectious mononucleosis". Again, from the purist's standpoint, how can a "mononucleosis" be infectious? It is better, in the reviewer's opinion, to use the old term "glandular fever." Epstein and Dameshek recently reported the case of an individual showing the signs of a meningo-encephalitic process with lymphocytes in the spinal fluid. This patient on further study was found to show the typical clinical and hematological features of glandular fever. These authors speculated regarding the possibility that some of the cases reported as "aseptic lymphocytic meningitis" might in reality be cases of glandular fever with lymphocytes in the spinal fluid.

In recent years, more knowledge has been accumulating concerning the exact nature of the so-called multiple myeloma. Various authors, including Jackson, Parker and Bethea, and Bross have demonstrated that "multiple myeloma" is in reality a neoplasm made up of plasma cells (plasmatocytoma) metastasizing from an original focus (tonsils, etc.) into the bone-marrow and causing the typical punched-out appearance of the bones seen by x-ray. Many authors consider the plasma cell to be an abnormal lymphocyte. (For discussion of plasma cell see Michels.) The occurrence of Bence-Jones proteinuria in plasmacytoma has been the occasion for some interesting studies (Bönniger; Wintrobe and Buell). Apparently the kidneys are frequently involved in the disease with resultant nephrotic changes and proteinuria of the peculiar type described by Bence-Jones.

2. *Disorders of the Reticulum Cells.* (See under Disorders of the Reticulo-Endothelial System.)

F. *Disorders of the Reticulo-Endothelial System.* The disorders of the reticulo-endothelial system are exceedingly interesting and their recognition in recent years has added much to our growing knowledge of certain hitherto obscure disorders.

A remarkable step in advance has been the recognition and detailed description of the so-called "*storage disorders*" of the reticulo-endothelial system (Derischanoff). Gaucher's disease is characterized by hepato- and splenomegaly, a slight degree of anemia, and pathologically by "foam cells" throughout the liver, spleen, bone-marrow, and lymph-nodes. The disease has been found to be due to the presence of large amounts of a fatty substance (kerasin) in the reticulo-endothelial cells of the entire body (Epstein). In the presence of xylol, alcohol, etc., which are used in the preparation of paraffin tissues, the fatty substance present in these cells becomes dissolved leaving a characteristic "foamy" appearance. Bone lesions are interesting and should always be looked for (Welt, Rosenthal and Oppenheimer). Splenectomy is of no avail in this generalized process which is frequently familial and usually found in Jewish families (Welt et al; Anderson). Closely allied to this disorder is xanthomatosis in which the same cells store large amounts of cholesterol (Rowland). The bone-marrow often becomes filled with large plaques of cholesterol-containing cells with resultant erosion and the formation of bone defects, usually seen in the skull. The reticuloendothelial cells of the skin and subcutaneous tissue also may become distended with this fatty substance resulting in the formation of the yellowish tumors called xanthomata. When these are present in the orbit, exophthalmos results. Christian described "defects in the membranous bones, diabetes insipidus and exophthalmos" in a few patients. Rowland did a great service by putting together all the various disorders associated with increased cholesterol storage in the reticuloendothelial cells and showed conclusively that Christian's syndrome (Hand-Schüller-Christian syndrome) was simply one manifestation of xanthomatosis. Lipoid histiocytosis (Niemann-Pick's disease) is an associated, very rare disorder of infants characterized by abnormal storage of various types of lipoid materials in the reticulo-endothelial cells of the entire body (Baty). Pick has described beautifully the skeletal lesions of these various disorders. Sosman has shown that the bone lesions, particularly of xanthomatosis, respond remarkably to x-ray therapy.

The proliferative lesions of the reticulo-endothelial system conform closely in type to those of the lymphoid system (Baserga). Benign proliferations occur in many infections notably in typhoid fever, tuberculosis, syphilis and generally in the more subacute or chronic infectious processes. The peripheral blood as noted above shows a monocytosis in these conditions. Monocytic angina ("infectious monocytosis") has been described (Schittenhelm). It is interesting in this connection to note that a bacterium has been isolated ("Bacterium monocytogenes") which is capable of producing a marked monocytosis in laboratory animals (Lang).

Neoplastic proliferations when localized may be benign (reticulo-endothelioma) or malignant (reticulum-cell sarcoma). In the past, these have been classed under the general class of

"lymphomata", although the tendency at present is to separate them from this group (Ewing). These reticulo-endothelial tumors are composed of masses of extremely large cells with irregular cytoplasmic processes. They respond readily to radiotherapy, radiosensitivity being a characteristic of all mesenchymal or blood cell tumors. A generalized proliferation of histiocytes throughout the body is manifested clinically as monocytic leukemia. (Vide supra.) The aleukemic form has recently been described by the author as "aleukemic reticulosis" (Dameshek).

The pathological picture of aleukemic reticulosis is characterized by generalized proliferation of histiocytes (reticular cells) with the laying-down of a great deal of reticulum. Giant cells are numerous. The pathological picture is in many respects closely similar to that seen in Hodgkin's disease, which is usually a disorder localized to a chain of lymph-nodes and the spleen. The reviewer in the above-mentioned paper raised the question as to whether Hodgkin's disease was not in reality a relatively localized reticulum cell proliferation. The proliferating cell in Hodgkin's disease does not appear to be of lymphoid origin but seems rather to be a much more primitive cell tending to differentiate into typical reticulum cells. A marked reticulum with resultant fibrosis is common. For these reasons, it is possible that Hodgkin's disease may be a type of reticulo-endothelioma, which if generalized, gives the picture of reticulosis. Most observers now feel that the disease is definitely neoplastic in nature, although its exact relationship to tuberculosis is still uncertain. Jackson and Parker have demonstrated the frequent finding of some form of tuberculosis in a large percentage of cases of Hodgkin's disease. It is possible to be sure that tuberculosis by initiating an originally benign reticulo-endothelial proliferation results occasionally in the neoplastic process called Hodgkin's disease. No advance in treatment has been made, x-ray treatment still being of definite value in ameliorating symptoms and possibly in prolonging life (Isaacs). Accurate diagnosis by biopsy of an accessible lymph-node should always be attempted. Treatment of a mass, node, or group of nodes in the absence of a definite diagnosis of a neoplastic process of the lymph-nodes is not to be recommended except under exceptional circumstances.

IV. Certain Disorders of the Spleen, The Splenic Anemias

The reviewer must confess very little enthusiasm for this once so important a subject. In his experience, the great majority of the cases of anemia with splenomegaly, originally called Banti's disease, have turned out to be myelogenous leukemia (aleukemic), Hodgkin's disease, or cirrhosis of the liver. A primary fibroadenitis of the spleen with leukopenia, hemorrhages from the stomach, and terminal cirrhosis of the liver, as described by Banti is apparently extremely rare (Fried; Howard and Mills). Certainly it is much rarer than one would gather from the number of cases clinically diagnosed as Banti's disease. In other words, the clinical diagnosis of Banti's disease should always be taken with a grain of salt and all possible efforts made to exclude the above-mentioned conditions. In most cases of continued enlargement of the spleen, leukopenia is a prominent feature and there is usually a distinct anemia together with some reduction of the blood platelets. This occurs in typhoid fever, malaria, cirrhosis of the liver, chronic syphilis, and in the residual splenomegaly following various infections. The possible antagonism between the spleen and the bone-marrow represents the rationale for splenectomy in cases of purpura hemorrhagica, aplastic anemia and congenital hemolytic icterus. In the latter disorder, splenectomy also results in the removal of the largest single mass of reticulo-endothelial cells. In infants and children, enlargement of the spleen develops at times with astonishing rapidity, particularly with infectious processes. Von Jaksch's anemia is now considered by most observers to be secondary to various infectious processes and associated with leukocytosis and splenomegaly. Syphilitic splenohepatomegaly is interesting because of the marked anemia, leukopenia and thrombocytopenia present in certain cases (Stokes). Therapy of those conditions characterized by splenomegaly, hepatic involvement, anemia, and leukopenia has advanced since the insistence of surgeons particularly at the Mayo Clinic upon splenectomy as a therapeutic measure. This procedure apparently aids in reëstablishing normal portal circulation and thus prevents the late sequelae such as hematemesis, etc. It also apparently ameliorates the anemia.

V. Certain Associated Disorders. Constitutional or Hereditary Tendencies

A few rare disorders which have been the occasion for some interesting papers may be mentioned in concluding this review. *Acute hematoporphyria* is manifested by photosensitivity of the skin, excretion of Burgundy-wine colored urine, at times by necrosing lesions of the fingers, at times by ascending Landry's paralysis (Mason and Farnham; Courville and Mason). It is apparently a disorder of pigment metabolism, in which large amounts of hematoporphyrin (the precursor of hemoglobin) circulate in the blood-stream. Another disorder of hemoglobin itself is *sulphhemoglobinemia* which, together with other closely-related conditions in which the circulating hemoglobin may be chemically altered, results in cyanosis and in insufficient oxygen-carrying capacity of the blood

(Harrop and Waterfield). In the idiopathic types of this disorder, the intestines may be at fault (enterogenous cyanosis) (Jones). *Hereditary hemorrhagic telangiectasis,* although not a "blood dyscrasia" but rather a disorder of arterioles and capillaries, may be mentioned here because it is at times mistaken for purpura hemorrhagica. The occurrence of blood-vessel lesions which superficially resemble petechial spots and the marked tendency to hemorrhage are the causes for this error. The reader is referred to the articles of Goldstein and Larrabee and Littman for excellent reviews of this interesting constitutional abnormality.

In conclusion, I cannot refrain from mentioning the constitutional or hereditary tendency which is particularly noticeable in diseases of the blood-forming organs. The familial tendency in pernicious anemia and combined system disease is well-known, the reviewer having observed several families in which at least two, in one case four members were afflicted with the disease. In these families, early greying of the hair and achlorhydria seem to be very common. Primary hypochromic anemia may be seen in the same family with pernicious anemia (Faber and Gram; Heath). Polycythemia vera is definitely hereditary in certain instances, and probably in many other cases if the constitutional factor is investigated. The sickle-cell trait is an hereditary familial condition as is congenital hemolytic icterus. Hemophilia is a standard hereditary disorder. Gaucher's disease and the other storage disorders of the reticulo-endothelial system are usually found in Jewish families. The reviewer has even observed typical chronic lymphatic leukemia in twin brothers, the disorder being recognized in both at about the same time; the blood cell counts were almost identical; and they died within a few months of each other.

REFERENCES

I. The Blood-Forming Organs

A. *The Bone-Marrow*

Arinkin, M. I.: Klin. Med. 7:135, 1929.
Arjeff, M. J.: Folia haemat. 45:55, 1931.
Custer, R. P.
(1): J. Lab. & Clin. Med. 17:951, 1932.
(2): Am. J. M. Sc. 185:617, 1933.
Dameshek, W.
(1): A Trephine for Biopsy of the Sternal Bone-Marrow. To be published.
(2): Primary Hypochromic Anemia (Erythronormoblastic Anemia). Am. J. M. Sc. 182:520, 1931.
(3): Some Types of "Primary" Anemia and Their Treatment. New Eng. J. Med. 205: 1093, 1931.
Doan, C. A.: J. Lab. & Clin. Med. 17:887, 1932.
Piney, A.: Recent Advances in Hematology. P. Blakiston's Son & Co. Phila. 1932.
Sabin, F. R.: Physiol. Rev. 8:191, 1928.
Seyfarth, C.: Deutsch. med. Wchnschr. 49:180, 1923.
Tempka, T. and Braun, B.: Folia haemat. 48:355, 1932.
Tuschinsky, M. D. and Kotlarenko, B. N.: Folia haemat. 46:235, 1932.

B. *The Lymphoid Tissue*

Maximow, A.: Text-Book of Histology. W. B. Saunders. Phila. 1930.
Piney, A.: Loc. cit.

C. *The Reticulo-Endothelial System*

Aschoff, L.: Verhandl. d. deutsch. path. Ges. 16: 107, 1913.
: Lectures on Pathology, N. Y. Paul B. Hoeber, Inc. 1924.
Bloom, W.: Folia haemat. 37:1, 1928.
Dameshek, W.
(1): Acute monocytic (histiocytic) leukemia. Arch. Int. Med. 46:718, 1930.
(2): Appearance of histiocytes in the peripheral blood. Arch. Int. Med. 47:968, 1931.
Epstein, E.: Virchow's Archiv. f. path. Anat. 281: 152, 1931.
Haldeman, K. O.: Arch. Path. 7:993, 1929.
Krumbhaar, E. B.: Internat. Clin. 2:280, 1925.
Maximow, A.: The Macrophages or Histiocytes, in Cowdry, E. V.: Special Cytology, N. Y. Paul B. Hoeber, Inc. 1932. Vol. II. P. 711.
Radt, P.: Med. Klin. 26:1888, 1930.
Schittenhelm, A.: Handbuch der Krankheiten des Blutes und der blutbildenden Organe, Berlin, J. Springer, 1925. Vol. II. P. 492.

II. The Blood Cells

A. *Derivation*

Dameshek, W.: Arch. Int. Med. 47:968, 1931.
Doan, C. A.: Medicine. 10:323, 1931.
Maximow, A.: Textbook of Histology, loc. cit.
Piney, A.: Loc. cit.

B. *Terminology*

Schilling, V.: The Blood Picture and Its Clinical Significance. American Edition, St. Louis, C. V. Mosby Co. 1929.

C. *The Schilling Index and Hemogram*

Cooke, W. E. and Ponder, E.: The Polynuclear Count. London. Griffin & Co., Ltd. 1927.
Farley, D. L., St. Clair, H., and Reisinger, J. A.: Am. J. M. Sc. 180:336, 1930.
Piney, A.: Loc. cit.
Reznikoff, P.: J. A. M. A. 93:963, 1929.
Schilling, V.: The Blood Picture. Loc. cit.

D. *The Monocyte, the Histiocyte, Supravital Studies*

Blackfan, K. D. and Diamond, L. K.: Am. J. Dis. Child. 37:233, 1929.
Cunningham, R. S., Sabin, F. R., Sugiyama, S., and Kindwall, J. A.: Bull. Johns Hopkins Hosp. 37:231, 1925.
Cunningham, R. S. and Tompkins, Edna H.
(1): Folia haemat. 42:257, 1930.
(2): Am. Rev. Tuberc. 17:204, 1928.
Dameshek, W.: Arch. Int. Med. 47:968, 1931.
Hall, B. E.: Folia haemat. 43:206, 1930.
Hertz, S. and Lerman, J.: J. Clin. Investigation. 11:1179, 1932.
Sabin, F. R.: Bull. Johns Hopkins Hosp. 34:277, 1923.
Tompkins, Edna H.: J. Lab. & Clin. Med. 17:921, 1932.

E. *The Blood Platelets*

Dameshek, W.: Arch. Int. Med. 50:579, 1932.
Olef, I.: Arch. Int. Med. 46:585, 1930.
Mackay, W.: Quart. J. Med. 24:285, 1931.
Pepper, O. H. P. and Farley, D. L.: Practical Hematological Diagnosis. Philadelphia and London, W. B. Saunders Co. 1933. P. 183.

F. *The Red Blood Cells*

Dameshek, W.: Primary Hypochromic Anemia III. To be published.
Keefer, C. S. and Yang, C. S.: Arch. Int. Med. 48:537, 1931.
Mettier, S. R. and Minot, G. R.: Am. J. M. Sc. 181:25, 1931.
Minot, G. R. and Heath, C. W.: Am. J. M. Sc. 183:110, 1933.
Rourke, M. D. and Ernstene, A. C.: J. Clin. Investigation. 8:545, 1930.
Snyder, L. H.: Blood Grouping in Relation to Clinical and Legal Medicine. Baltimore, Williams & Wilkins Co. 1929.
Steinberg, B.: Arch. Path. 9:876, 1930.
Wiener, A. S.: Am. J. M. Sc. 181:605, 1931.
: Am. J. M. Sc. 186:257, 1933.

III. Disorders of the Blood-Forming Organs

A. *Associated Physiological Factors*

B. *Outline for Study of a Patient*

Bloomfield, A. L. and Polland, W. S.: J. A. M. A. 92:1508, 1929.
Duke, W. W.: Arch. Int. Med. 42:533, 1928.
Haden, R. L.: J. Lab. & Clin. Med. 17:843, 1932.
Osgood, E. E. and Haskins, H. D.: Laboratory Diagnosis. Philadelphia, P. Blakiston's Son & Co. 1931.
Price-Jones, C.: Guy's Hosp. Rep. 4:10, 1924.
Sato, A. and Yoshimatsu, S.: Am. J. Dis. Child. 29:301, 1925.
Wintrobe, M. M.: J. Lab. & Clin. Med. 17:899, 1932.

C. *Bone-Marrow Disorders*

1. *The Red Blood Cells*

(a) *The Anemias*

(aa) *Classification*

Dameshek, W.: New Eng. J. Med. 205:1093, 1931.
Haden, R. L.: Arch. Int. Med. 49:1032, 1932.
Osgood, E. E.: Arch. Int. Med. 37:685, 1926.
Wintrobe, M. M.: Proc. Soc. Exp. Biol. & Med. 27:1071, 1930.
Witts, L. J.: Lancet. 1:495, 549, 601, 1932.

(bb) *The Macrocytic Anemias*

Baker, B. M., Bordley, J. III, and Longcope, W. T.: Am. J. M. Sc. 184:1, 1932.
Birkeland, I. W.: Medicine. 11:1, 1932.
Castle, W. B.: Observations on the etiologic relationship of achylia gastrica to pernicious anemia. I. Am. J. M. Sc. 178:748, 1929.
Castle, W. B. and Townsend, W. C.: II. Am. J. M. Sc. 178:764, 1929.
Castle, W. B., Townsend, W. C. and Heath, C. W.: III. Am. J. M. Sc. 180:305, 1930.
Castle, W. B. and Rhoads, C. P.: Lancet. 1:1198, 1932.
Cheney, G. and Niemand, F.: Arch. Int. Med. 49:925, 1932.
Fouts, P. J. and Zerfas, L. G.: J. A. M. A. 101:188, 1933.
Greenfield, J. G. and O'Flynn, Eliz.: Lancet. 2:62, 1933.
Morris, R. S., Schiff, L., Burger, G. and Sherman, J. E.: J. A. M. A. 98:1080, 1932.
Murphy, W. P.: J. A. M. A. 98:1051, 1932.
Richter, O., Meyer, A. E., and Ivy, A. C.: J. A. M. A. 98:1623, 1932.
Strauss, M. B. and Castle, W. B.
(1): Am. J. M. Sc. 184:655, 1932.
(2): New Eng. J. Med. 207:55, 1932.
Strauss, M. B., Taylor, F. H. L. and Castle, W. B.: J. A. M. A. 97:313, 1931.
Sturgis, C. C. and Isaacs, R.: J. A. M. A. 93:747, 1929.

(cc) *The Hypochromic Anemias*

Alt, H. L.: Illinois M. J. 64:72, 1933.
Dameshek, W.
(1): Am. J. M. Sc. 182:520, 1931.
(2): J. A. M. A. 100:540, 1933.
(3): To be published.
Davies, D. T.: Lancet. 2:385, 1931.
Haden, R. L.: J. A. M. A. 99:1398, 1932.
Heath, C. W., Strauss, M. B. and Castle, W. B.: J. Clin. Invest. 11:1293, 1932.
Kaznelson, P., Reimann, F., and Weiner, W.: Klin. Wchnschr. 8.1:1071, 1929.
Minot, G. R. and Castle, W. B.: Ann. Int. Med. 5:159, 1931.
Murphy, W. P.: Arch. Int. Med. 51:656, 1933.
Wintrobe, M. M. and Beebe, R. T.: Medicine. 12:187, 1933.
Witts, L. J.: Practitioner. 127:439, 1931.

(dd) *Secondary Anemias*

(ee) *Aplastic Anemias*

Dameshek, W.: New Eng. J. Med. 205:1093, 1931.

(ff) *Anemias of Children*

Cooley, T. B., Witwer, E. R. and Lee, P.: Am. J. Dis. Child. 34:347, 1927.
Ferguson, J. A.: Am. J. Path. 7:277, 1931.
Kato, K. and Downey, H.: Folia haemat. 50:55, 1933.
Morquio, L. and Volpe, G.: Rev. franç. de Pédiat. 9:153, 1933.

b. *Polycythemia Vera*

Brown, G. E. and Giffin, H. Z.: Arch. Int. Med. 46:705, 1930.
Forkner, C. E.: J. Clin. Investigation. 11:807, 1932.
Gaisböck, F.: Klin. Wchnschr. 2:699, 1923.
Holfelder, H. and Reisner, A.: Strahlentherapie. 47²:274, 1933.
Morris, R. S.: J. A. M. A. 101:200, 1933.
Stone, C. T., Harris, T. H. and Bodansky, M.: J. A. M. A. 101:495, 1933.

2. *The White Blood Cells*

(a) *Agranulocytosis*

Beck, Regena C.: Arch. Int. Med. 52:239, 1933.
Dameshek, W.: New Eng. J. Med. 209:1054, 1933.
Dameshek, W. and Ingall, M.: Am. J. M. Sc. 181: 502, 1931.
Doan, C. A.: J. A. M. A. 99:194, 1932.
Foran, F. L., Sheaff, H. M. and Trimmer, R. W.: J. A. M. A. 100:1917, 1933.
Jackson, Henry Jr., Parker, Frederic Jr., Rinehart, J. F. and Taylor, F. H. L.: J. A. M. A. 97:1436, 1931.
Jackson, Henry Jr., Parker, Frederic Jr., Taylor, F. H. L.: Am. J. M. Sc. 184:297, 1932.
Reznikoff, Paul: J. Clin. Investigation. 9:381, 1930.
Roberts, S. R. and Kracke, R. R.: J. A. M. A. 95:780, 1930.

(b) *Myelosis* (Myelogenous Leukemia): see "Leukemias".

3. *The Blood Platelets*

a. *The Platelet Deficiencies and the Hemorrhagic Disorders*

b. *Non-Thrombocytopenic Purpuras*

Frank, E.: In Schittenhelm's Handbuch (loc. cit.) Vol. II, p. 451.
Glanzmann, E.: Jahr. f. Kinderh. 91:391, 1920.
Stockton, M. R. and Franklin, G. C. H.: J. A. M. A. 96:677, 1931.

c. *Hemophilia*

Birch, C. La F.
(1): Proc. Soc. Exper. Biol. & Med. 28:752, 1931.
(2): J. A. M. A. 97:244, 1931.
(3): J. A. M. A. 99:1566, 1932.
Brown, R. L. and Albright, F.: New Eng. J. Med. 209:630, 1933.

D. *The Leukoses* (Leukemias)

Clough, P. W.: Bull. Johns Hopkins Hosp. 51:148, 1932.
Dameshek, W.
(1): Arch. Int. Med. 46:718, 1930.
(2): Folia haemat. 49:64, 1933.
Forkner, C. E. and Scott, T. F. McN.: J. A. M. A. 97:3, 1931.
Gloor, W.: München. med. Wchnschr. 77:1096, 1930.
Isaacs, R.: J. Lab. & Clin. Med. 17:1006, 1932.
: Am. J. Roentgenol. 24:648, 1930.
Jackson, Henry Jr., Parker, Frederic Jr., and Robb, G. P.: Folia haemat. 44:30, 1931.
Kato, K. and Brunschwig, A.: Arch. Int. Med. 51:77, 1933.
Steinberg, C.: Henke and Lubarsch's Handbuch der speziellen pathologischen Anat. und Hist. Berlin. J. Springer. 1:76, 1926.

E. *Disorders of the Lymph-Nodes*

1. *Disorders of the Lymphoid Cells*

Bönniger, M.: Deutsch. med. Wchnschr. 59:770, 1933.
Bross, K.: Folia haemat. 45:137, 1931.
Epstein, S. H. and Dameshek, W.: New Eng. J. Med. 205:1238, 1931.
Ewing, James: Neoplastic Diseases. W. B. Saunders Co. Phila. and London. 3rd ed. 1928.
Jackson, Henry Jr., Parker, Frederic Jr. and Bethea, J. M.: Am. J. M. Sc. 181:169, 1931.
Longcope, W. T.: Am. J. M. Sc. 164:781, 1922.
Michels, N. A.: Arch. Path. 11:775, 1931.
Wintrobe, M. M. and Buell, M. V.: Bull. Johns Hopkins Hosp. 52:156, 1933.

2. *Disorders of the Reticulum Cells:* see Disorders of the Reticulo-Endothelial System.

F. *Disorders of the Reticulo-Endothelial System*

Anderson, J. P.: J. A. M. A. 101:979, 1933.
Baserga, A.: Haematologica (Rec.). 4:61, 1933.
Baty, J. M.: Am. J. Dis. Child. 39:573, 1930.
Christian, H. A.: Contributions to Medical and Biological Research. N. Y. Paul B. Hoeber. 1:390, 1919.
Dameshek, W.: Folia haemat. 49:64, 1933.
Derischanoff, S. M.: Frankfurt. Ztschr. f. Path. 41:184, 1931.
Epstein, E.: Virchows Arch. f. path. Anat. 281: 152, 1931.
Ewing, James: Neoplastic Diseases (loc. cit.).
Isaacs, R.: Am. J. Roentgenol. 24:648, 1930.
Parker, Frederic Jr., Jackson, Henry Jr., Bethea, J. M. and Otis, F.: Am. J. M. Sc. 184:694, 1932.
Lang, F. J.: Folia haemat. 36:31, 1928.
Pick, L.: Am. J. M. Sc. 185:453, 1933.
: Am. J. M. Sc. 185:601, 1933.
Rowland, R. S.: Arch. Int. Med. 42:611, 1928.
Schittenhelm, A.: Handbuch (loc. cit.). Vol. II, p. 540.
Sosman, M. C.: Am. J. Roentgenol. 23:581, 1930.
Welt, Sara., Rosenthal, N. and Oppenheimer, B. S.: J. A. M. A. 92:637, 1929.

IV. Certain Disorders of the Spleen. The Splenic Anemias

Fried, B. M.: New Eng. J. Med. 207:595, 1932.
Howard, C. P. and Mills, E. S.: J. A. M. A. 99: 162, 1932.
Stokes, J. H.: Modern Clinical Syphilology. W. B. Saunders Co. Phila. 1921.

V. Certain Associated Disorders. Constitutional or Hereditary Tendencies

Courville, C. and Mason, V. R.: Arch. Neurol. and Psychiat. 25:848, 1931.
Dameshek, W., Savitz, H. A., and Arbor, B.: J. A. M. A. 92:1348, 1929.
Faber, K. and Gram, H. C.: Arch. Int. Med. 34: 827, 1924.
: Acta Med. Scand. 34: 107, 1929 (Suppl.).
Goldstein, H. I.: Arch. Int. Med. 48:836, 1931.
Harrop, G. A. and Waterfield, R. L.: J. A. M. A. 95:647, 1930.
Heath, C. W.: Am. J. M. Sc. 185:365, 1933.
Jones, C. A.: Chapter on Enterogenous Cyanosis in Cecil's Textbook of Medicine. W. B. Saunders Co. Philadelphia and London. 1933. P. 1060.
Larrabee, R. C. and Littman, D.: New Eng. J. Med. 207:1177, 1932.
Mason, V. R. and Farnham, R. M.: Arch. Int. Med. 47:467, 1931.

CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

EDITED BY RICHARD C. CABOT, M.D.
F. M. PAINTER, A.B., ASSISTANT EDITOR

CASE 20101

PRESENTATION OF CASE

A fifty-one year old English housewife entered the hospital complaining of swelling of localized areas of the body of six weeks' duration.

At the age of fifteen she began to have typical attacks of bronchial asthma with wheezing, difficult inspiration and expiration, dyspnea, and nocturnal orthopnea. These symptoms persisted until at the time of entry the asthma was constant the whole year round regardless of what region she was in, although it was worse at some times than at others. Morphia was begun at the onset of the disease and was used occasionally for some years. During the present attack it had been used daily in doses of one-half grain with only partial relief. Three years before entry she developed frank hemoptysis on several occasions, severe night sweats, dyspnea and orthopnea, as well as a persistent cough. She entered a hospital, where she developed marked cyanosis on exertion which had persisted. She also became aware of marked palpitation on exertion, accompanied by dull precordial pain. Six weeks before admission edema of the ankles was noticed. A short time before entry a new type of edema developed. Various parts of her body, such as the feet, legs, thighs, back, abdomen and face, swelled very rapidly at times, the swelling lasting for a period of several hours. The swollen areas were red, had a tingling sensation, and were quite sensitive to touch. At the same time she developed a steady non-radiating, gnawing, moderately severe mid-epigastric pain which was unrelieved by food or soda. There was no change in her bowel habits. For the past two months she had remained in bed. There had been no loss in weight.

Family history. Her father died of jaundice at the age of eighty-two. Her mother was living and well at eighty-four. One sister and two brothers were living and well. One sister died of appendicitis. There was no history of tuberculosis. Several members of the family had cancer.

Marital history. She had been married thirty-six years. Her husband and one daughter were living and well. She had had one miscarriage several years before entry.

Past history. She was born in England and lived there for twenty years, then in Canada for a few years, and for the remainder of her life had lived in Vermont. She had had pneumonia several times and an attack of rheumatic fever thirty years before entry.

Physical examination showed a poorly nourished middle-aged woman lying propped up in bed, dyspneic, with an asthmatic type of breathing. She was perspiring freely. The cervical veins were distended. Her lips were moderately cyanotic. A few small cervical lymph glands were palpable. Her chest was emphysematous in shape, nearly rigid in the inspiratory position. The costal margins retracted with inspiration. The percussion note was not so hyperresonant as was expected. The breath sounds were harsh, with greatly prolonged expiration. There were many coarse moist râles, especially at the bases. The heart was moderately enlarged. The left border of dullness was 9.5 centimeters, the right 3 centimeters from the midsternal line. The supracardiac dullness was 6 centimeters. The sounds were not remarkable except for a tic-tac quality. The rate was 70. The blood pressure was 150/110. The abdomen was distended and tympanitic. There was tenderness without spasm in the right upper quadrant over an area of dullness taken to be an enlarged liver four fingerbreadths down, although the edge could not be felt because of tenderness. There was massive pitting edema of the legs.

The temperature was 98°. The respirations were 28.

Examination of the urine was negative. Examination of the blood showed a red cell count of 5,300,000 with a hemoglobin of 75 per cent. The white cell count was 13,500, with 88 per cent polymorphonuclears, 10 per cent lymphocytes and 2 per cent large mononuclears. The sputum was small in amount, thick, mucopurulent, and contained many partly disintegrated pus cells; no tubercle bacilli. The non-protein nitrogen was 32 milligrams. The renal function was 25 per cent at the end of fifteen minutes with a total of 40 per cent at the end of the test.

X-ray examination of the chest showed a diaphragm which was low, markedly irregular and limited in excursion. Both costophrenic angles and the right cardiophrenic angle were obliterated. There was a triangular area of dullness occupying the costovertebral angle on the right side in the region of the middle lobe. Both lung fields were grossly abnormal. There were linear and mottled areas of dullness scattered over both lung fields and in the left apex there were areas of diminished density which had the appearance of cavities. There was a large cavity which occupied the entire right apex and extended down to the arch of the aorta. There were no fluid levels seen in any of these cavities. The heart was grossly enlarged in all diameters. The supracardiac shadow was increased. The respiratory excursion of the heart

was absent. Fluoroscopic examination revealed absence of cardiac pulsations. Examination of the films brought in by the patient showed startling variation in the size of the heart. In a film taken on June 7, 1930, the heart measured 13 centimeters, 5.8 to the right and 7.2 to the left. In May 1931 the heart measured 14 centimeters, 6 to the right and 8 to the left. In June 1932 it measured 14.3 centimeters, 4.5 to the right, 9.8 to the left. In December 1932 it measured 12 centimeters, 3.7 to the right, 8.3 to the left. On June 26, 1933, it measured 16.7 centimeters, 6.3 to the right and 10.4 to the left. The only change in the lung was at the right base, and in several of the films it was difficult to determine where the right border of the heart stopped and where the pathology in the lung began.

It was believed that she had pericardial effusion and two taps were attempted, one in the fourth intercostal space 8.5 centimeters to the left of the midsternal line and another in the third intercostal space just to the right of the sternum. No fluid was obtained from either of these taps and it was felt that on both occasions the needle entered the ventricular wall. She was given moderate doses of digitalis and salyrgan without any marked diuretic effect. Her cardiac symptoms increased. Her heart rate continued to be slow until the twelfth night, when it reached 100 and cyanosis and dilatation of the veins became more marked. She died early the following morning.

Differential Diagnosis

Dr. Frederick T. Lord: In view of the character of the attacks we may assume that the patient has had bronchial asthma since the age of fifteen. Also I understand from this summary that she had been taking morphia for a considerable period and more recently in doses of a half grain, so I presume she had morphia addiction. The second important feature in respect to the story of the present illness is the disturbance beginning three years before admission with hemoptysis, night sweats, shortness of breath, orthopnea and persistent cough which lasted until her death. A third feature of the story is the obvious circulatory disturbance with shortness of breath, palpitation and cyanosis, and some pain, not adequately characterized, in the precordial region. In addition as a minor manifestation there was the occurrence over different parts of the body of swellings which would appear very rapidly and subside, lasting over a period of several hours. The areas were red, had a tingling sensation and were sensitive to touch. I am inclined to attribute that swelling to angioneurotic edema. The pain in the epigastrium is inadequately described. I am inclined to think in view of the other manifestations of circulatory failure that this pain was due to circulatory disturbance.

As far as the past history is concerned, there is a history of pneumonia on several occasions and rheumatic fever thirty years ago. We have to accept these at their face value because the manifestations are not described.

On physical examination she is said to have had an asthmatic type of breathing. I am surprised that in view of that no sibilant râles were found on examining the chest. She evidently had emphysema. The chest was "emphysematous in shape". I am not familiar with this expression. I presume it means the lung was in a state of inflation due to an excess of air, as it goes on to say that the chest was rigid in the inspiratory position.

The retraction of the costal margins with inspiration is of special interest, as under normal conditions the costal margins move away from the median line during this phase of respiration. In explanation it may be suggested that the fixation of the lung in the inspiratory phase prevents further expansion by the intercostal muscles and permits unopposed action of the diaphragm with consequent narrowing of the lower thoracic aperture. Moreover, the low fixed position of the diaphragm as seen in the x-ray would favor this, in accordance with Hoover's contention that the more nearly its curve approximates a plane the greater its mechanical advantage in control of the costal margin to which it is attached.

The examination of the heart has already been given. She had some hypertension, evidently enlarged liver, with edema.

It would be interesting in regard to the physical examination to know whether she had a Broadbent's sign. She has other indications of disturbance that might have given rise to Broadbent's sign.

In the x-ray films, in addition to the linear and mottled areas of increased density there are ring shadows with the appearance of cavities. The objection to the conclusion that these are cavities is the absence of fluid level, but in our experience both at operation and autopsy such ring shadows have often turned out to be cavities even though they show no fluid level, and I am inclined to regard them as cavities.

In view of the apparent immobility of the heart in the long axis of the body by x-ray examination, I should like to know whether it is also fixed laterally. An electrocardiogram might help to decide this, if there were lack of axis deviation of the QRS complexes on changing the patient's position.

Dr. William B. Breed: There was no electrocardiogram.

DR. LORD: With respect to the conclusions, I make the diagnosis of bronchial asthma with some confidence because I do not think it can be refuted at autopsy. I have a similar assurance with respect to morphinism and angioneurotic edema. About the rest of the diagnosis I am not so confident. I think she had a bronchopulmonary infection. In spite of the negative sputa, in consequence of the story of hemoptysis and night sweats and the x-ray picture pulmonary tuberculosis is uppermost in my mind. One also has to consider with respect to the pulmonary situation a silicosis or asbestosis. This patient came from Vermont, but she is a housewife and so far as any evidence is concerned has never been exposed to dust. One has also to consider, I presume, a luetic disturbance. Nothing that I have in the record indicates that a complement fixation test was done; or is that an omission by design?

DR. BREED: I believe it was not done in this hospital, but it had been done in Vermont and was negative.

DR. LORD: Other causes of bronchostenosis than bronchial asthma should be considered. We are increasingly alive to the importance of this group in patients who give a history of wheezing and have sibilant râles on examination. Syphilis of the trachea and bronchi may give rise to this complex, but I think we can exclude it here. Malignant disease of the tracheobronchial tree may also be responsible, and I think we cannot exclude that here, though it is unlikely on account of the long duration of the asthma. Still another condition to be mentioned is bronchiolitis obliterans, and pressure on the bronchi from without may cause asthmatic symptoms. These disturbances are however unlikely, and it is probably asthma with superimposed infection. As to the nature of this infection, blastomycosis may be considered, but only rarely occurs without skin lesions and is hardly tenable here. I am inclined to think that the pulmonary disturbance is bronchial asthma and that the pulmonary process is tuberculosis.

With respect to the circulatory disturbance, she has heart disease and congestive failure. Whether her heart condition is rheumatic we do not know. There certainly is no evidence that it is endocarditis, although it may be. There is no evidence on physical examination that it should be so regarded. All the indications would seem to point on physical examination and x-ray to an adhesive pericarditis, and I am inclined to think that this has gone beyond mere obliteration of the cavity, which might account for the absent pulsations; but the fixation of the heart would suggest that it involves the neighborhood too, with adhesion of the pericardium to the neighborhood, the mediastinum, the pleura, the diaphragm, and possibly the chest wall.

CLINICAL DISCUSSION

DR. GEORGE W. HOLMES: I can add little to that very good description of the x-ray that was read, but I might point out one or two things. First, the very definite dullness at the left apex is probably due to a destructive process in this apex. Then in the lateral view the region in which the process is seen is the region of the middle lobe and it extends through into the anterior mediastinum. At least there is no normal tissue visible between the sternum and the anterior border of the heart, and that again would point to the same conclusion to which Dr. Lord apparently came, that this thing might be tuberculosis of the lung with extension into the mediastinum and involvement of both the mediastinum and the pericardium.

In differentiating enlarged hearts and fluid in the pericardium the curves of the normal heart are of some value. With fluid they usually become straight lines. Then in the lateral view the space back of the heart, between the heart and the spine, is not obliterated. With fluid it usually is obliterated. So the evidence we have here is more in favor of adhesive pericarditis than it is of fluid in the pericardium, although of course there might be encapsulated fluid. If we could be sure of these cavities that would almost make the diagnosis; I think with the other evidence we have, and with cavity formation, it would be tuberculosis. These areas do resemble cavities, but I would not be absolutely certain that they are.

DR. J. H. MEANS: What is that perfectly round black hole behind the manubrium?

DR. HOLMES: It may be a cavity or an area of overexposed emphysematous lung.

DR. BREED: I cannot say that we had any feeling of confidence about the clinical diagnosis in this case, but I should like to say a word about our ante mortem opinion. Having seen the autopsy, I shall not talk too much about the case. We thought she had a secondary pulmonary infection with tuberculosis, and we felt that she had cavity formation on that basis. She had no Broadbent's sign. The heart sounds were not distant. I think that we should not have felt there was fluid in the pericardium except on the evidence of the x-ray in Vermont, and particularly in view of the change of the heart's size during the past three years. We did a paracentesis in an attempt to relieve some of the strain on her circulatory system as much as for diagnosis. It was a dry tap.

DR. WILLIAM D. SMITH: Dr. Breed was good enough to ask me to see this case. I also saw the autopsy, so that my remarks will be limited.

The patient had a perfect background for emphysema heart, or cor pulmonale. There were two or three things that made me dissatisfied to stop there. In the first place her heart rate was slow, regular, not rapid (70-80), though she ob-

viously had congestive failure with signs of extreme venous congestion. Furthermore, on physical examination she had a heart that was very, very big; and while one can have a big heart in cor pulmonale, I have not been in the habit of seeing them as huge as this one.

In the next place, if this was a dilated heart due to back pressure and failure, and if the heart was so big because it was dilated, then it was extraordinary that she should have a relatively slow and regular heart rate, and it was a little queer that there was no murmur, nothing to suggest tricuspid insufficiency due to a dilated right heart. Also, her neck veins were strikingly congested. They stood out like cords. All this made me unwilling to stop at pulmonary heart disease and I felt that she probably had adhesive pericarditis, possibly mediastinopericarditis. She had also, presumably, tuberculosis. I did not think for a moment on physical examination that she had pericardial effusion, but after talking with the x-ray people and looking at the films I admitted that she might have pericardial effusion and was willing to have an attempt made at paracentesis; but Dr. Breed and I both agreed that there was nothing on physical examination to suggest that she had a pericardial effusion.

DR. MEANS: Because of these features which Dr. Smith has just mentioned, I should like to suggest the remote possibility of a terminal thrombosis of the pulmonary artery. They bear some resemblance to the case, Dr. Mallory, that you and I had three or four years ago.

DR. DONALD S. KING: Did she have a history of epidemic influenza?

DR. SMITH: I think not.

DR. KING: Some men recently have said that these pulmonary fibroses follow epidemic influenza. I have been looking for cases and have not found them. I thought perhaps this might be one.

DR. BREED: I was sure she did not have rheumatic heart disease.

DR. SMITH: I should agree to that. There was not a particle of evidence of mitral stenosis or of any rheumatic heart disease.

A PHYSICIAN: How much temperature did she have?

DR. BREED: None.

CLINICAL DIAGNOSIS (FROM HOSPITAL RECORD)

Tuberculosis of lungs, pleura and pericardium.

DR. FREDERICK T. LORD'S DIAGNOSES

Bronchial asthma.
Pulmonary emphysema.
Pulmonary tuberculosis.
Bronchopulmonary infection.
Adhesive pericarditis.

ANATOMIC DIAGNOSES

(Bronchial asthma.)
Pulmonary emphysema.
Organized bronchopneumonia, multiple foci.
Pulmonary arteriosclerosis.
Cor pulmonale.
Puncture wounds of the heart.
Hemopericardium.
Hydrothorax, bilateral.
Ascites.
Central necrosis of the liver.
Kyphosis, slight.
Chronic fibrous pleuritis.

PATHOLOGIC DISCUSSION

DR. TRACY B. MALLORY: The autopsy was somewhat of a surprise because no tuberculosis whatever was found and the very large cavities turned out to be emphysematous sacs the largest of which was five centimeters in diameter. The intervening lung tissue between the emphysematous areas showed a marked degree of fibrosis of a very peculiar character, so that the huge emphysematous blebs surrounded by fibrous walls gave a picture that proved indistinguishable from tuberculous cavities.

The sections are very interesting. This first section is an eosin methylene blue stain of an area of marked fibrosis. With this stain you can see nothing but fibrous scarring and can get no idea how it occurred. With the elastic tissue stain it becomes much more evident how this has been brought about. Here is one of those fibrous areas, a small one, one centimeter in size which is made up of fifty or more alveoli completely collapsed, and fused together by fibrous tissue; but the elastic tissue of the original alveolar walls persists and allows us to make out their outline. In the neighborhood of the scars we get the most marked emphysematous lesions, for the most part with thin walls, but in other places showing very thick walls. Everywhere the pulmonary arteries show a marked degree of sclerosis. The majority of the bronchi show a certain amount of plugging with mucus and a definite narrowing of the lumina and thickening of the musculature, all typical asthma. The distribution of the emphysema varies in the different lobes. It was most marked in the two upper ones, but some emphysema was present in every lobe.

DR. BREED: Will you say a word about the size of the heart wall, particularly of the right ventricle?

DR. MALLORY: The heart was hypertrophied, weighing 400 grams. The left ventricular wall was normal or a little reduced in size. The right measured 14 millimeters, as against a left of 16 millimeters. The right side was practically as large as the left, between three and four-fold hypertrophy.

The liver was not enlarged, but showed a slight

passive congestion and a moderate degree of central necrosis.

The pericardial tap had punctured the ventricle and there was a very small amount of free blood in the pericardial cavity.

I think this case is of very considerable interest in relation to a study of emphysema recently published by Loeschke from the University of Mannheim in Germany. Loeschke has been working on emphysema for a number of years with a very unusual technic. In every case in which he thought there was a probability of emphysema he has embalmed the body before doing the autopsy, then removed the entire thoracic cage with the lungs inside it and then made multiple frozen sections through the lungs. He studied literally hundreds of cases in that way, a type of work, needless to say, that it would be impossible to do in this country. As a result of that work he has come to the conclusion that the most important etiologic factor in emphysema is the spatial readjustment within the thorax. The commonest type is an anteroposterior enlargement of the thorax generally from kyphosis, with compensatory anterior and upward motion of the sternum. He shows in his publication pictures of innumerable thoraces with kyphosis of various levels and scoliosis of various degrees, and shows that in the portions of the chest that would be enlarged by the deformity emphysema is present; in the opposing portions there is no emphysema.

Another mode of pathogenesis fitting the same theory is the spatial readjustment within the thorax when large groups of alveoli are completely destroyed and collapsed. The neighboring alveoli about the scarred area are forced to dilate to fill up the space.

Scattered throughout every lobe of both these lungs we have innumerable scars varying from a millimeter to a centimeter in size which are made up of collapsed alveoli, sometimes ten or fifteen, sometimes one hundred or two hundred, all compressed down to a diameter of less than a centimeter. The corresponding dilatation in the surrounding alveoli is exactly that which Loeschke predicts and which he believes is the main cause of emphysema.

It is interesting that one of the standard theories of emphysema is a loss of elastic tissue in the lungs, and I have never seen so much demonstrable elastic tissue as there was in this case. Even in the walls of the emphysematous alveoli there is a large number of elastic fibrils. Loeschke has also found the same thing and feels that the elastic tissue is by and large the most resistant structure of the alveolar wall; that all other elements of the alveolar wall disappear before the elastic tissue does.

Of course this patient had asthma, and one might assume that the emphysema was due to the asthma. We have now nearly twenty cases of known asthma coming to autopsy in this hospital and this is the first one that has shown a significant grade of emphysema. Loeschke, working back from emphysema, came to the same conclusion, that bronchial asthma alone without other pulmonary complications was in itself a very unimportant cause, if ever a cause of emphysema.

DR. LORD: I should like to know about the pericardium.

DR. MALLORY: Except for the hemopericardium it was entirely negative. I have no explanation for the variation in the size of the heart or for the lack of pulsation of the various chambers.

DR. HOLMES: The movements of the heart may have been obscured by the limitation of the diaphragm.

About those emphysematous blebs, when I hear the term bleb I think of something on the surface. They were not on the surface too, were they?

DR. MALLORY: They were on the surface and internal. The largest ones were on the surface.

DR. HOLMES: Some of them were actually cavities within the lung?

DR. MALLORY: Yes.

A PHYSICIAN: Was there much sclerosis of the pulmonary artery to cause the enlargement of the veins in the neck?

DR. MALLORY: The main pulmonary artery was not greatly involved. The smaller ones showed a marked degree of sclerosis, but it is just as probable that the sclerosis and the right heart failure were both secondary to the same lesion.

DR. BREED: I take it that this shadow under the sternum in the x-ray film might be one of the emphysematous blebs with the cavity there.

DR. HOLMES: It is possible, but I should not feel certain.

CASE 20102

PRESENTATION OF CASE

DR. CHARLES F. WARREN:* This is the case of a married Italian laborer who came to the Outpatient Department first at the age of twenty-seven, a year and a half before his admission to the wards, and gave the following history.

For two years previously he had been intermittently employed mixing silica dust and liquid soap in the manufacture of abrasive soap. Four months before the visit he had had to give up work for two months on account of dyspnea and pain in his chest. He got no worse and was able to go back to work two months later, but had dyspnea and pain more frequently. Two days before the visit he was again unable to continue because of the dyspnea and chest pain. Physical examination at that time was

*Recently senior interne on the West Medical service.

essentially normal except for the fact that his respirations were 27 and he had some scattered areas of dullness in his chest. Expansion of the chest was poor, and at the left base there was some decrease in tactile fremitus and in breath sounds. Dr. E. M. Chapman saw him at that time and immediately started him on ammonium chloride and advised him to discontinue his work. Clubbed fingers were noted at a second examination three weeks later; otherwise the findings were the same as before. A series of chest x-rays was taken at that time.

He got along fairly well at home for seventeen months except that he had a marked tendency to upper respiratory infections accompanied by dyspnea and cyanosis and some chest pain. He also had a markedly diminished vital capacity. Five weeks before his entry to the wards he suddenly caught cold, as he said, with increase of all the symptoms he had had previously. There was no fever at that time, but he was put to bed. Two weeks before entry he began to run a fever said to be 99° to 102.4°, usually more marked in the afternoon. One week before he came in he had a sudden attack of marked dyspnea and cyanosis which lasted until his doctor gave him a hypodermic injection six hours after the onset. He was advised to come into the hospital then, but he did not do so until he had a second attack on the day of entry, persisting until it was relieved by two hypodermic injections. He finally made up his mind to come to the Emergency Ward.

When he was seen there he was in marked respiratory distress, and extremely cyanotic. The neck veins were very full and distended. There were moist râles throughout both chests, with dullness, bronchial breathing, egophony, increased tactile fremitus, and friction rub over the right lower chest. The heart was not remarkable except for its somewhat globular shape. The blood pressure was 120/80, the temperature 104°, the pulse 170, the respirations about 45.

Because of his extremely poor condition he was immediately placed in an oxygen tent. We were able to group a pneumococcus type IV from his sputum, but his white blood cell count was only 12,500. After spending the night in an oxygen tent, the next morning his temperature was normal, his pulse 92 and his respirations 27. He continued to improve a little for a few days. On the sixth day he reached probably his maximum period of well-being, when he was out of the oxygen tent for six hours. After that when he was out of the tent for an hour his temperature would go to 101° or 102° and his respirations increased. The story from this period until death on the 23rd day was one of less and less ability to be out of the oxygen tent. Finally he required an increasing amount of oxygen saturation in the tent to keep him comfortable. He developed some edema of the ankles and some pleuritic pain on the left side. The signs of consolidation at the right base cleared up, but there remained dullness and scattered râles throughout the chest without the definite consolidation that he had at entry. His red blood count was 3,900,000, his hemoglobin 70, his Hinton test negative. His white blood cell count was usually 9000 to 10,000. We were never able to discover any tubercle bacilli in the sputum. There seemed to be at his weakest no change in pulse and respirations so long as he was kept in the oxygen tent. He died rather suddenly in his sleep.

Clinical Discussion

Dr. Aubrey O. Hampton: At the first x-ray examination at the time of his first visit to the Outpatient Department we thought he did not have the characteristic appearance of ordinary silicosis; that is, he did not have small miliary nodules scattered over the periphery of the lungs. He had only thickened lung tissue. In the films taken two months, five months and a year later there is no definite change that we can see, although the x-ray exposure necessary to penetrate the lung tissue had penetrated the heart and shows the vertebrae. Even with an x-ray exposure of this type the lungs still look as though there was not enough air or as though it had been replaced by edema. I think that given a patient with edema elsewhere I should be perfectly content with calling this picture edema and increase in pulmonary pressure. The only definite evidence we had of fibrosis was the adherent diaphragm.

In this picture taken at the time he entered the wards, however, the findings are almost identical with those of the other men who died of the same disease. We could not see any aërated lung at all in the middle and lower portions of the lung. The whole lung picture was that of diminished air content without any definite lines. That is the last examination.

Dr. Warren: An investigation three weeks after his first visit to the Outpatient Department disclosed that five out of six similar cases in men who had been doing the same kind of work in the same plant had ended in death from acute silicosis.

The discharge diagnosis was primary silicosis. I believe he may or may not have had pneumonia before or when he came in, but that seemed to disappear before he died.

Dr. Earle M. Chapman: This case is the third one we have followed and the second one in which we obtained autopsy findings of silicosis. All cases had been observed in the industry of making a cleanser which is silica mixed with soap. The disease in this case was quite acute, in contrast to the usual slowly progressing ones we see. The reason for this probably is that the alkaline mixture of the soap hastens the reaction of fibrosis in the lungs.

It is interesting that at the time of his first x-ray examination they were unable to make a

diagnosis of silicosis. The x-ray showed diffuse density but no areas of consolidation. The right side of the heart from the midline to the right border was out 5.3 centimeters. We interpreted that as showing right-sided cardiac enlargement due to resistance in the pulmonary vascular bed. A clinical diagnosis of silicosis was made, and we followed him for eighteen months, to the time of his death.

DR. TRACY B. MALLORY: What was the interval between the last exposure in the factory and the time of death?

DR. CHAPMAN: He had been exposed for twenty-nine months in the industry. The last time he was exposed in the industry was, I believe, twenty-two months before entry. He went back to work after that, but had an ordinary job without exposure to silica dust.

CLINICAL DIAGNOSES (FROM HOSPITAL RECORD)

Silicosis.
Bronchopneumonia.

ANATOMIC DIAGNOSES

Acute pulmonary silicosis.
Silicosis of bronchial, mesenteric and retroperitoneal glands.
Pulmonary edema.
Acute purulent tracheitis and bronchitis.
Cardiac dilatation and hypertrophy, right, very slight.
Hydropericardium.
Splenomegaly.
Hepatomegaly.
Tuberculosis (?) of splenic glands.
Chronic fibrous pleuritis.
Chronic cholecystitis.
Cortical adenoma of adrenal.

PATHOLOGIC DISCUSSION

DR. MALLORY: One of the interesting features of the case is that pathologically this seems to be a very acute lesion in spite of the interval since the last exposure. In other words we seem to be dealing with a toxin which continues to acutely progressive injury for extraordinary periods of time after it has once been absorbed into the body.

I have two pairs of lungs here which are rather large to pass around, but I hope you will look at them as you go out. These on my right are from the first case we autopsied here and show a more chronic type of process than today's case does. They show peculiar deep scars which seem to divide the lung into a score of lobes much as the scars of healed gummata produce the hepar lobatum of syphilis. In today's case there is practically none of that deep scarring. Instead we have a diffuse induration, fairly uniform throughout both lungs, though most marked in the lower lobes, where the consistency is practically that of leather. The diffuse fibrosis was so marked that the miliary nodules usually found in silicosis could not be made out grossly, though microscopically we have been able to find typical ones.

I will show you first a section from the older case, the one in which the process is more finished. In this you can see that the interlobar septa, which in a perfectly normal lung are so thin that they may readily be overlooked, are here very broad, dense and the most obvious thing in the section. In the midst of these broad bands of fibrous tissue are round spherical masses which stain bright pink, entirely free from nuclei, and apparently consisting only of collagen in which are imbedded minute doubly refractile silica granules. Those are the miliary silicotic nodules which are characteristic of the disease. They tend to be most numerous in the lymphatics, and mechanical blocking of the lymphatics may become a factor in the pulmonary edema which often develops.

This section is from today's case and shows the same thickening of the interlobular septum, not quite so marked as in the preceding case but nevertheless very definite. There are very few of the spherical masses. In this case there is considerable hyperplasia of the lymphoid tissue, probably an actual new formation of lymph nodules well out in the periphery of the lung. The most striking feature of this lung is the presence in every alveolus of large amounts of pink staining fluid, an extreme grade of edema apparently with a very high protein content. Another interesting finding is the presence of epithelium in all the alveoli. Normally no epithelium can be seen in the lungs. Some people have even doubted its existence. In this case almost every alveolus shows a definite low cuboidal epithelial lining. Sometimes it is stripped off the walls and hangs in little festoons in the lumen of the alveolus.

The process, as usual, extended beyond the lungs to the lymph nodes, and they contained the characteristic silicotic nodules in much greater numbers than the lung itself. These lesions are often extremely difficult to distinguish from healed miliary tubercles; but only in a few nodes from the splenic pedicle did we find a few lesions genuinely suggestive of tuberculosis.

A PHYSICIAN: Had he a big spleen?

DR. MALLORY: The spleen was enlarged, and in the corpuscles there was marked fibrosis. Whether that was an integral part of the process I do not know, because one sees it very frequently in other lesions.

A PHYSICIAN: Were there any silicotic nodules in the bone marrow?

DR. MALLORY: No. The marrow shows only hyperplasia.

A PHYSICIAN: Do you think the cyanosis was due to thickening of that alveolar lining?

DR. MALLORY: It may have been due to that. I think the extraordinarily uniform edema perhaps is a little more apt to be the cause of it. He must have had edema nearly as marked as this for months before he died. I am rather inclined to think that the appearance of the epithelial lining is secondary to that. One does see epithelial lining of this type appear under conditions where the lungs lose their aërating function, for instance in organizing pneumonia.

DR. WYMAN RICHARDSON: I think the man's temperature chart is interesting. Although in heart failure there is often a fever, it is not so marked as in this case.

DR. MALLORY: I must admit that I do not know of any other condition to bolster up the theory that anoxemia may cause hyperthermia, and yet this case strongly suggests it in the way the chart jogs up and down with each deprivation of oxygen.

DR. CHAPMAN: The fever in congestive failure is accounted for by lessened peripheral heat loss from the sluggish circulation.

DR. MALLORY: In this man the heart weighed 300 grams, which I think is just about normal for his weight of 140 pounds. The right ventricle wall did appear relatively thick, 6 millimeters against a normal of about 3.5 millimeters. I think he had some degree of right hypertrophy.

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CANCER OF THE PROSTATE

IN this issue of the *Journal* appears a significant contribution by Doctor Frederick L. Hoffman on Cancer of the Prostate and Prostatic Diseases. The significance of this article lies not only in the figures showing the increase of deaths from these causes (an increase which may be more apparent than real), but in the fact that the importance of prostatic cancer is recognized by some one who is not a urologist.

As with cancer elsewhere in the body, the successful treatment of cancer of the prostate depends largely upon early recognition of the condition. Like cancer of the stomach, prostatic cancer often gives no symptoms until it has progressed to a stage where treatment can be only palliative. The symptoms most commonly encountered may be divided into two classes —pain, caused by extension of the growth along the pelvic lymphatics or by metastases to the spine, and symptoms due to bladder dysfunction. These latter may be due to urinary obstruction alone or to obstruction plus infection. Not infrequently there are no local symptoms at all; the patient becomes cachectic and even uremic without having suffered any pain. In the large majority of cases, cancer of the prostate is of relatively slow growth; it seems probable that the disease frequently exists in a recognizable state for several years before causing symptoms severe enough to lead the patient to consult a doctor.

The obvious conclusion to be drawn from these observations is that palpation of the prostate by rectum should constitute a part of every physical examination in men of fifty or over. If this were done routinely, many cases of prostatic cancer (and rectal as well) would be detected early, or at least much earlier than would be the case if such examinations were postponed until definite prostatic symptoms occurred. The stony hardness of the malignant prostate is striking; any gland presenting an unyielding, hard structure should be suspected of malignancy. Such prostates may be smaller than the average gland; the cancerous prostate is often not obstructive until a late stage, unless the condition is accompanied, as it frequently is, by hypertrophy.

Unfortunately there exists a strong feeling of pessimism as to the value of treatment in this disease. Many physicians choose to follow a laissez faire policy in these cases, believing that this is the best that can be done. It is true that the number of cases of prostatic cancer that have been cured is pitifully small, but this is largely due to the fact that the patient does not come to the surgeon until his disease is far advanced. If women with cancer of the breast were not operated upon until the axillary glands were thoroughly infiltrated with growth, the percentage of cures would be extremely low.

Radical removal of the prostate and vesicles in the earlier cases, and in the more advanced cases prostatic resection plus radiation, offer great relief from suffering and an occasional check to the growth which is the next thing to a cure. Every year of comfort added to the life of the patient with prostatic cancer is worth fighting for.

Let us hope that Doctor Hoffman's article will be widely read, and will be the beginning of a campaign against a disease which causes extreme suffering and a lingering illness, and is apparently increasing in prevalence.

COÖRDINATED VOLUNTARY HEALTH WORK

THE National Health Council held its annual meeting at the Hotel Roosevelt, New York City, February 28, 1934, and elected Colonel Theodore Roosevelt, former Governor General of the Philippines, president.

The Council is composed of seventeen national health organizations, and, according to the statement in the *New York Times,* has for its general purpose the prevention of disease by acting as a clearing house for member organizations, unifying health education procedure, preventing duplication of work, and developing economies of administration.

Colonel Roosevelt will enter upon his duties immediately. He explained that all of the member health groups are working toward a common end although the specific object of each may seem to be different. He felt that great service will be rendered, and advances made if the work of the member groups can be coördinated. He believes that each one, for example the child health, the mental hygiene, the tuberculosis, the cancer, the heart, and all the rest of the groups, may conduct surveys simultaneously, and take on coördinated teamwork which will be outside of government activities. Although he recognizes the necessity of government work in crises, the opinion was expressed that if more is done by voluntary agencies, and less by the government, the general result will be more satisfactory. This we believe to be sound because the effect will be a more general interest in health problems by the people, and a growing feeling of individual and community responsibility. It may be that the progress in the tuberculosis and cancer campaigns has been rapid because of the awakened interest of the masses in these movements. Where the interest of the great majority of the people can be aroused in any matter of personal concern, confidence in scientific medicine seems to advance. This office of Colonel Roosevelt carries no compensation, and it is gratifying to have this intelligent layman take this important position.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

HOFFMAN, FREDERICK L. LL.D. Tulane University 1911. Consulting Statistician, Prudential Insurance Co. Member, American Cancer Research Association. Director, American Society for the Control of Cancer. His subject is "Cancer of the Prostate and Prostatic Diseases." Page 507. Address: 133 South 36th Street, Philadelphia, Pennsylvania.

MCCANN, JAMES C. A.B., Ph.D., M.D. Harvard University Medical School 1924. F.A.C.S. Surgeon, St. Vincent Hospital, Worcester. His subject is "Peptic Ulcer. Its Surgical Management." Page 512. Address: 390 Main Street, Worcester, Massachusetts.

CONWELL, H. EARLE. M.D. University of Alabama School of Medicine 1915. F.A.C.S. Orthopedic Surgeon, Employees' Hospital of Tennessee Coal, Iron & Railroad Company, Fairfield, Alabama. His subject is "Some Problems Frequently Encountered in the Treatment of Recent Fractures." Page 522. Address: Tennessee Coal, Iron & Railroad Company, Employees' Hospital, Fairfield, Alabama.

BIGELOW, GEORGE H. A.B., M.D. Harvard University Medical School 1916. Formerly, Massachusetts State Commissioner of Public Health. Now Director, Massachusetts General Hospital. Address: Massachusetts General Hospital, Boston, Massachusetts. Associated with him is

LOMBARD, HERBERT L. A.B., M.P.H., M.D. Bowdoin Medical School 1915. Director, Division of Adult Hygiene, Massachusetts Department of Public Health. Address: 100 Nashua Street (10th Floor) Boston, Massachusetts. Their subject is "Change in the Massachusetts Cancer Trend." Page 526.

BARTON, WALTER E. B.S., M.D. University of Illinois College of Medicine 1931. Assistant Physician, Medical Service, Worcester State Hospital. Address: Worcester State Hospital, Worcester, Massachusetts. Associated with him is

FREEMAN, WILLIAM. B.Ch.E., D.N.B., M.D. Boston University School of Medicine 1929. Pathologist at the Worcester State Hospital, and the Worcester Hahnemann Hospital, Worcester, Massachusetts. Assistant in Pathology, Boston University School of Medicine. Consulting Pathologist, Stephen Henry Gale Hospital, Haverhill, Massachusetts and Nantucket Cottage Hospital, Nantucket, Massachusetts. Address: P. O. Box 489, Worcester, Massachusetts. Their subject is "Pericardial Hemorrhage Complicating Scurvy." Page 529.

DAMESHEK, WILLIAM. M.D. Harvard University Medical School 1923. Associate Physician, Beth Israel Hospital. Physician, Research Division of the Boston State Hospital. Physician, Boston Dispensary. Physician to the Blood Clinics of the Beth Israel Hospital and Boston Dispensary. Instructor in Medicine, Tufts College Medical School. His subject is "Progress in Hematology (1929-1933)." Page 531. Address: 371 Commonwealth Avenue, Boston, Massachusetts.

MISCELLANY

THE APPOINTMENT OF DR. R. C. WIGGIN

At the recent meeting of the Massachusetts Memorial Hospitals, Dr. Ralph C. Wiggin was appointed Surgeon-in-Chief to the Hospitals.

Dr. Charles P. Howard has resigned this position after thirty-six years of service, but will act as Con-

sultant in Surgery. Dr. Howard will continue as professor of surgery of the Boston University School of Medicine.

Dr. Wiggin served in the World War as captain in the Medical Corps with the unit sent to France by the Memorial Hospitals.

UNWARRANTED CURATIVE CLAIMS

"If you suffer from influenza, bronchitis, malaria, stomach complaints, and certain other diseases, do not trust to whisky in the treatment of your illness," says Dr. F. J. Cullen of the Federal Food and Drug Administration. "Whisky has some value," says Dr. Cullen, "as a stimulant to the appetite and as a general stimulant, but it has no use in the cure or treatment of any disease."

Recently the Government seized 499 cases of "Old Grand-dad" whisky, shipped by the American Medicinal Spirits Co., Inc., Louisville, Ky., to the firm's place of business in Chicago, Ill. The whisky was grossly misbranded with remedial claims for a number of diseases, including pulmonary conditions, stomach complaints, la grippe, "typhoid and other low fevers". The label went on to say that the whisky could also be used to render the system immune from various diseases and externally, for ulcers.

Another recent seizure initiated by the Food and Drug Administration removed from the market several hundred bottles of "Old Nectar" whisky, which was labeled with remedial claims for bronchitis, influenza, and other maladies. The whisky was shipped from a New York City warehouse to a Baltimore branch of the firm. The Government charged that the whisky was falsely and fraudulently labeled as to its curative claims and that additionally it did not comply with the requirements of the United States Pharmacopoeia.

Recently, Dr. Cullen states, the Federal court for the northern district of Illinois assessed a fine of $100 upon Fridolin Pabst, trading as Pabst Chemical Company, Chicago, Ill., for shipping in interstate trade a nostrum known as "Pabst's Okay Specific." The preparation contained no ingredients which, according to medical opinion, would be effectual in the cure of gonorrhea and gleet, yet the circulars accompanying the article made curative claims with regard to these diseases. The medicine was misbranded in that the labels on the bottles bore false and fraudulent claims as to the remedial nature of the goods. Quantities of "Pabst's Okay Specific" were shipped to Beaumont, Texas, and San Juan, Puerto Rico. The Government had previously seized the goods.

The recent prosecution of Pabst was not the first one. Several years ago he was fined for a similar offense. In the recent case the court stated that if the defendant, who pleaded guilty, committed another such violation of the Federal food and drugs act, the court would be disposed to impose a jail sentence.

"Persons suffering from a venereal disease should immediately seek competent medical advice as to the treatment of the disease," states Dr. Cullen. "There are free clinics in all cities for the treatment of those unable to pay. Sufferers should not rely upon the advertised claims of charlatans who have worthless nostrums to sell. Nor should they be misguided by false and fraudulent label claims for the goods, nor by assertions made in circulars which commonly accompany these preparations. During the 27 years of enforcement of the national pure food and drug law, the government has seized large numbers of drug preparations falsely recommended as being worthwhile treatments or cures for venereal diseases."—*Bulletin, U. S. Dept. of Agriculture.*

CORRESPONDENCE

"VITAMIN D MILK IN THE TREATMENT OF INFANTILE RICKETS"

February 28, 1934.

Editor, *New England Journal of Medicine,*

The death of Dr. Hess has made me reluctant to comment on the letter from him that appeared in the December 7th issue. In justice to the studies reported by Dr. Gittleman and me, I feel that I must call attention to the following points:

In the paper on "Vitamin D Milk in the Treatment of Infantile Rickets, A Clinical Assay," we drew the following conclusions:

1. The definite curative action of as little as 40 Steenbock units daily shows vitamin D milk to be our most effective antirachitic agent.
2. At the levels fed there was no significant difference in effectiveness between vitamin D milk prepared by direct irradiation and vitamin D milk produced naturally by feeding cows irradiated yeast.
3. The apparent discrepancy between the minimal clinically effective dose of vitamin D in the form of vitamin D milk and in the form of cod-liver oil or viosterol requires further investigation.

These conclusions were based upon a study carried out in infants that were hospitalized throughout the entire period of observation. They were kept in a room from which actinic rays of the sun were excluded, by keeping the windows closed and the shades drawn. The rooms were freely aërated at night. Each child was observed for a control period of two to three weeks to rule out spontaneous healing from accidental treatment received previous to admission to the hospital. As further controls, some children were fed vitamin D milk while others were given equal amounts of plain milk.

As Dr. Hess has pointed out in his letter, we do not question the effectiveness of irradiated milk, but

we do question the right of Dr. Hess and his collaborators to draw conclusions as to the relative effectiveness of irradiated milk and milk produced by yeast feeding, without testing the two milks, side by side, at the same levels. We feel that we have carried out such a study.

Dr. Hess maintains that it is impossible to draw even tentative conclusions from our work because the observations were made during the months of April, May and June, and in one instance, even extended into the first week of July. We agree most heartily that clinical studies such as those carried out by Hess and Lewis, in which patients remain at home, under such supervision and control as can be given by visiting nurses, should be discontinued about the end of March, in order to avoid the possibility of spontaneous healing. After that time such children are almost certain to get healing amounts of sunshine. In studies such as ours, however, in which all patients are hospitalized, this need for discontinuance disappears. With the preliminary observation period each child serves as its own "untreated control" to rule out the possibility of healing as the result of previous exposure to sunlight or other inadvertent antirachitic medication.

The presence of our two "untreated controls" which were discarded because of spontaneous healing, might cast doubt upon the value of our treated cases if it were not for the fact that each treated case served as its own "untreated control." Because of this the "untreated controls" merely emphasize the importance of the preliminary observation period.

Dr. Hess insists that an adequate demonstration of the relative potency of the two forms of vitamin D milk requires not only that the two forms of vitamin D milk be fed over an equal period of time and at the same level, but also that they be fed simultaneously at a level of vitamin D which just suffices to bring about healing within a definite period and in addition, at one which just fails to produce healing. He points out that such a study is reported by Hess and Lewis in an article which appeared in the *J. A. M. A.* of July 15, 1933. In the interest of justice, I desire to state that our paper was complete and had been submitted for publication before the appearance of Dr. Hess's paper, and that I was abroad at the time and did not see the article until the latter part of August.

A careful analysis of the data given in their paper fails to show that the conditions stated by Drs. Hess and Lewis themselves, have been complied with. Yeast milk was fed at a level of 60 units per day and evidence of healing appeared in all but one child at the end of four weeks, and in this child healing appeared at the end of six weeks. One may seriously question whether 60 units of vitamin D in the form of yeast milk, does represent a "minimal level." In their paper of July 15, 1933, Hess and Lewis stressed the fact that the milk which was fed to the children was repeatedly assayed for its vitamin D content. Unfortunately, this cannot be said of the milk used in previous studies by Hess and his collaborators. Hess, Lewis, MacLeod and Thomas, in a table given in their paper, show that when 60,000 units of vitamin D are fed to cows daily, in the form of irradiated yeast, the milk secreted contains approximately 160 units of vitamin D to the liter. Dr. C. A. Smith, who has had a very extensive experience in feeding irradiated yeast to cattle, informs me that it requires at least 110,000 to 130,000 units of vitamin D in the form of irradiated yeast to yield milk which contains approximately 160 units to the liter, when cows are producing 30 to 40 pounds of milk daily. This would seem to indicate that the milk which Dr. Hess fed in experiments previous to the paper of July 15, 1933, was probably weaker than he calculated. This suspicion is justified by the statement of Drs. Hess and Lewis in their report of July 15, 1933, in which they state, "In our previous experiments assays were not carried out on the identical preparations, which were given to the infants." Thus, it would seem that their early cures were obtained with milk poorer in vitamin D than they calculated.

We obtained definite healing with 40 units of Vitamin D in the form of yeast milk, and it is not unlikely that even this does not represent the "minimal dose." Drs. Hess and Lewis in their paper of August 20th, state that for an exact comparison of the two milks, a study in which the two types of therapy are carried out at the same time and under similar conditions, is necessary. We believe that we have followed their specifications more carefully than they did themselves. We also feel very strongly that the controls were of such a nature as to exclude completely any beneficial effect upon the rachitic condition other than that which was due to the vitamin D milk itself. Similar studies carried out during the winter months are desirable and are being carried out now.

Sincerely yours,

BENJAMIN KRAMER, M.D.

OBITUARY

RESOLUTIONS ON THE DEATH OF DR. JEREMIAH J. CORBETT ADOPTED BY THE NEW ENGLAND PHYSICAL THERAPY SOCIETY

Dr. Jeremiah J. Corbett was born in Peabody, Massachusetts, on August 28, 1877. He died in Santa Fe, New Mexico, on August 24, 1933, while on a vacation trip.

He was educated in the public schools of Peabody and at St. Francis Xavier's College, receiving his medical degree from the Harvard Medical School in 1906.

He specialized in diseases of the eye, ear, nose and throat and was, at the time of his death, Ophthalmic Surgeon-in-Chief of the Boston City Hospital; Surgeon-in-Chief, Eye, Ear, Nose and Throat Department of the Malden Hospital, and Consulting Ophthalmic and Aural Surgeon, Whidden Memorial Hospital, Everett.

He was a charter member of the New England

Physical Therapy Society. Other medical societies of which he was a member included the American College of Surgeons, American Medical Association, American Academy of Ophthalmology and Otolaryngology, New England Ophthalmological Society, New England Otological and Laryngological Society, the Massachusetts Medical Society and the Malden Medical Society.

He was an interested attendant at the meetings of our Society and took a prominent part in the discussions, particularly when subjects were presented which related to his specialty in medicine. He contributed much by his knowledge of the scientific application of physical therapy in the realm of his specialization and applied these principles of treatment in many of his cases. He also showed his appreciation of the value of these measures of treatment by referring cases to physicians specializing in physical medicine. His writings on these subjects have been of value.

Be it resolved that in the passing of Dr. Jeremiah J. Corbett, the New England Physical Therapy Society has lost a member who, by his high character, his scholarly attainments, his kindliness, his spirit of coöperation and his knowledge of physical measures of treatment, was, from its inception, one of its most valued Fellows.

To his bereaved widow and son, we extend our sincerest sympathy.

Be it further resolved that a copy of these resolutions be sent to his immediate family, to the *New England Journal of Medicine*, and that a copy be spread upon the records of the New England Physical Therapy Society.

WILLIAM D. MCFEE, M.D.,
Committee on Resolutions.

RECENT DEATHS

CHURCHILL—JOHN DARLING CHURCHILL, M.D., of 63 Court Street, Plymouth, Massachusetts, died at the Jordan Hospital, Plymouth, March 2, 1934.

Dr. Churchill was born in Minneapolis in 1874, the son of Frederick Lee Churchill and Mary Diman Churchill, both of whom were formerly of Plymouth. After graduating from Harvard College he entered the Harvard Medical School and was awarded his medical degree in 1900, and joined the Massachusetts Medical Society in 1906. After graduating in medicine he practiced in Wyoming and Oklahoma for a few years before settling in Plymouth. He had served as physician to the Plymouth county jail for more than thirty years.

He is survived by his mother; his widow, Elizabeth Churchill; a son, Frederick; a sister, Mrs. Thomas L. Small, and a brother, Gilman Churchill.

CARVILL—LIZZIE MAUD CARVILL, M.D., of Somerville, Massachusetts, with an office at 82 Commonwealth Avenue, Boston, died at her home, February 25, 1934.

Dr. Carvill was born at Lewiston, Maine, in 1873. She was educated at the Chauncy Hall School, Boston, and Tufts College, and graduated in medicine from the Tufts College Medical School in 1905.

She carried on a general practice for several years, and then devoted herself to ophthalmology. She joined the Massachusetts Medical Society in 1905, and was also a Fellow of the American Medical Association. She was a member of the New England Ophthalmological Society, and served on the staff of the Massachusetts Eye and Ear Infirmary.

She is survived by a brother, Sewall A. Carvill of Somerville, and two nephews.

NOTICE

RADIO HEALTH MESSAGES

MARCH, 1934

Sponsorship: Public Education Committee of the Massachusetts Medical Society and Massachusetts Department of Public Health.

Courtesy WBZ. Fridays, 4:30 P.M.

March

16 Fractures
23 How to Keep the Well Child Well
30 Résumé of the Year's Work

HEALTH QUESTION BOX

Sponsored by Massachusetts Department of Public Health. Fridays, 4:40 P.M.

RADIO HEALTH FORUM

Queries from the public are answered under the sponsorship of the Department of Public Health.

Courtesy WEEI. Fridays, 5:00 P.M.

Questions on Health and Prevention of Disease may be sent to Radio Health Forum, State Department of Public Health, State House, Boston.

SPECIAL

Courtesy WEEI. Fridays, 1:15 P.M.

Glimpses into the History of Public Health in Massachusetts together with the Functions and Activities of the Massachusetts Department of Public Health, Blended with Classical Music.

REPORTS AND NOTICES OF MEETINGS

MASSACHUSETTS GENERAL HOSPITAL CLINICAL STAFF MEETING

The clinical staff of the Massachusetts General Hospital held its February meeting in the Moseley Memorial Building on Thursday, February 15, at 8:15 P.M. Dr. C. Langdon Parsons was chairman of the meeting.

The meeting opened with the presentation of an unusual case of cholelithiasis in a 63 year old housewife who had entered the hospital complaining of

abdominal pain of four days' duration. The pain was at first in the right upper abdominal quadrant and later shifted to the right lower quadrant. The physical examination was essentially negative except for a slight icteric tint in the sclerae and spasm in both upper and lower right abdominal quadrants. The icteric index on two occasions was 8. The Graham test showed "no filling". The diagnosis was between appendicitis and cholecystitis. Operation was scheduled and just before it the patient vomited a small gallstone. At operation a small gallbladder with numerous adhesions was found associated with a markedly dilated common duct. Many stones were removed from both common and hepatic ducts, after which the ampulla was dilated and the wound closed without catheter drainage of the common duct. Shortly after the operation the patient passed numerous gallstones in her stool. The stones were displayed mounted on cards.

Dr. Robert R. Linton spoke on the diagnosis of the hemorrhagic tendency in obstructive jaundice. He first gave a short introduction concerning the history and the importance of the condition from a surgical point of view. He spoke of the decrease in the mortality rate from hemorrhage in obstructive jaundice during the past decade, and explained that it was partly due to the better preparation of the patients prior to operation, to the use of multiple stage operations in very ill patients, and to the choice of the best anesthetic. Furthermore, by the use of the test for the sedimentation rate of the blood it has been possible to predict which patients were likely to bleed and so prepare them with especial care.

He reviewed the most common tests used to detect the hemorrhagic diathesis of obstructive jaundice. These were the coagulation time, the bleeding time, the blood fibrin level, the duration and the degree of the jaundice. All of these were shown to be of little or no value in the detection of the bleeding tendency. The test for the sedimentation rate of the blood in these cases, which he described in 1930, has been used with more success than any of the others, and at present, according to him, is the best available indication we have of this dreaded complication of obstructive jaundice. He pointed out that it is not the perfect test, but that it is of great aid in dealing with these patients.

The next speaker was Dr. C. M. Jones, who discussed the "Medical Significance of Gallbladder Disease." He emphasized the fact that in this disease the history is as important or more important than the laboratory data. Whether surgery is to be done is often determined by the patient's history. Physical examination is notoriously disappointing for diagnosis, especially if done in the period between attacks. An x-ray of the gallbladder region may show the presence of stone in 10 per cent of the cases. The Graham test is more significant, with an accuracy of about 80 per cent in good hands. The precautions to be observed in performing the test were discussed. The Graham test is of little value in cases of long-standing jaundice and it is seldom of value in cases of obstructive jaundice. Its significance is questionable in cirrhosis and false positives are also not infrequently encountered in cases of duodenal ulcer. A positive Graham test (no filling) may sometimes be obtained in cases with diarrhea when the oral method of administration is used. The indications for duodenal drainage and its value for the diagnosis of obscure or doubtful cases were discussed. However, no laboratory procedure is infallible.

The differential diagnosis of gallbladder disease was next considered. One should keep in mind the following conditions: coronary disease, right-sided pleurisy, renal colic, duodenal ulcer, and rarely lead colic, tabes, and herpes. Cirrhosis of the liver sometimes gives right upper quadrant pain with or without jaundice. Catarrhal jaundice and hemolytic jaundice should be kept in mind. The indications for surgery were discussed and it was concluded that the surgeon should always consider whether sufficient relief will be obtained to warrant operation.

The final speaker was Dr. Leland S. McKittrick who discussed some surgical aspects of gallbladder disease. The importance of the history in making the diagnosis was emphasized. The attacks of gallstone colic characteristically occur more frequently at night, and are commonly of varying intensity. The pain may occur anywhere in the abdomen and its radiation, when present, is suggestive. The conditions that may be confused with gallstone colic are renal colic, frequently; appendiceal colic, uncommonly, and angina pectoris which should always be considered. Duodenal ulcer sometimes gives the same picture, but the history and an x-ray study of the gastro-intestinal tract are very helpful.

The Graham test was described in relation to stones in various positions in the biliary tract. The gallbladder is not expected to "fill" in cases with stones impacted in the ampulla of that organ. The important points in the symptomatology of common duct stone were mentioned. Frequently recurring attacks of chills and fever are very typical. In the diagnosis of malignancy with biliary obstruction, Courvoisier's law is more frequently applicable than is commonly taught especially if one describes the jaundice as painless and progressive.

Dr. McKittrick concluded with a discussion of the pathology and treatment of acute pancreatitis. In this condition one finds blood-tinged fluid in the abdomen, an injected peritoneum, and scattered areas of fat necrosis. The pancreas is markedly distended within its capsule. The pain is very severe and seldom relieved by morphine. Vomiting is early. There is generalized abdominal tenderness especially over the pancreas, and evidence of shock. Operation is indicated, the most important procedure being the cutting of the pancreatic capsule to relieve the pressure. The illness may continue for weeks and months, and the mortality is high.

After an interesting discussion by Drs. Means, White, and Whitaker, the meeting was adjourned.

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the office of the Boston Tuberculosis Association, 554 Columbus Avenue. Boston, on Tuesday, March 20, 1934, at 12 noon. The speaker will be Thomas J. O'Brien, M.D., Visiting Physician at the Boston City Hospital; Professor of Clinical Medicine at Tufts College Medical School. His subject will be "Medical Legislation." All physicians are cordially invited to attend. The usual luncheon will be served.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

The Middlesex East District Medical Society will meet at the Bear Hill Club in Stoneham at eight o'clock on Wednesday, the fourteenth of March. Dr. William R. Morrison will address the meeting on "Stomach Surgery," illustrating his talk with a film. A buffet luncheon will follow.

ALLAN R. CUNNINGHAM, M.D., *Secretary.*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Hospital Amphitheatre (Van Dyke Street entrance), Tuesday evening, March 13, at 8:15 o'clock.

Clinical and Experimental Observations on the Effect of Total Thyroidectomy

1. Samuel A. Levine. "The Rationale for Total Thyroidectomy in the Treatment of Intractable Heart Disease."
2. Eugene C. Eppinger. "The Effect of Total Thyroidectomy on the Response to Adrenalin in Man."
3. Philip Shambaugh. "Observations on 'Experimental Angina Pectoris' in Animals."
4. Morton G. Brown and Margaret Sawyer. "The Action of Secreted and Injected Adrenalin Before and After Total Thyroidectomy."
5. Max T. Schnitker. "Skin Temperature Reactions Before and After Total Thyroidectomy."
6. Elliott C. Cutler. "Clinical Results Following Total Thyroidectomy."

JOHN HOMANS, M.D., *Secretary.*

THE CUTTER LECTURE ON PREVENTIVE MEDICINE

BY KARL LANDSTEINER, MEMBER OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH, NEW YORK CITY

Immunochemical Specificity

Friday, March 16, 1934, at the Harvard Medical School, Amphitheatre Building E, 5 P.M.

These lectures are given annually under the terms of a bequest from John Clarence Cutter, whose will provided that the lectures so given should be styled the Cutter Lectures on Preventive Medicine and that they should be delivered in Boston and be free to the medical profession and the press.

The medical profession, medical and public health students, the press and others interested are cordially invited to attend.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

The next meeting of the New England Ophthalmological Society will be held on Monday, March 12, at the Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston.

PROGRAM

9:00 A.M. Clinic and Operating Room.
11:00 A.M. Neuro-Ophthalmological Conference.
2:00 P.M. Clinico-Pathological Conference.
3:00 P.M. Interesting Muscle Cases.

Evening Program, 8:00 o'clock

Clinical Cases.

Intermedin in the Diagnosis of Melanotic Sarcoma. Dr. Charles Lund.

Operations on Ocular Muscles in Exophthalmos. Professor A. Bielschowsky.

The Course on Ocular Muscles by Dr. Bielschowsky will be given on the 13th, 14th, 15th and 16th, at 7:00 P.M.

BENJAMIN SACHS, M.D., *Secretary.*

THE NEW ENGLAND ROENTGEN RAY SOCIETY

The March meeting will be held Friday night, March 16, 1934, at the Boston Art Club, Boston, Mass., at 8:00 P.M. (Round Table Conference).

Dinner will be served at 6:30 P.M. for $1.00 a plate.

SCIENTIFIC SESSION

Table No. 1—"Conference on the Roentgenology of the Gastro-Intestinal Tract." Drs. Hampton, Schatski and Holmes.
Table No. 2—"General Clinic, Chest Cases, Skull Cases and Bone Cases." M. C. Sosman, M.D.
Table No. 3—"Roentgen Diagnosis of Heart Disease." George Levene, M.D., Frank E. Wheatley, M.D.
Table No. 4—"The Esophagus and Gastro-Intestinal Tract in Infants and Children." E. C. Vogt, M.D.
Table No. 5—"Roentgen and Radium Therapy." Richard Dresser, M.D.

T. R. HEALY, M.D., *Secretary.*
370 Marlborough Street, Boston, Mass.

MASSACHUSETTS MEMORIAL HOSPITALS

The regular monthly meeting of the Surgical Section will be held in the Trustees' Room of the hospital on Friday, March 9, 1934, at 12 o'clock noon.

Dr. Ensio K. F. Ronka will address the members on "The Medical Wisdom of Mark Twain."

RALPH C. WIGGIN, M.D., *Secretary.*

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

March 9—William Harvey Society will meet in the auditorium of the Beth Israel Hospital, Boston, at 8 P.M.

March 9—Massachusetts Memorial Hospitals. See page 561.

March 12—New England Ophthalmological Society. See page 561.

March 13—Harvard Medical Society. See page 561.

March 16—New England Roentgen Ray Society. See page 561.

March 16—Cutter Lecture on Preventive Medicine. See page 561.

March 20—South End Medical Club. See page 561.

March 23—New England Pediatric Society will meet in Boston. For information address Dr. Gerald Hoeffel, Secretary, 319 Longwood Avenue, Boston.

April 13, 20 and 27—Salmon Memorial Lectures. See page 443, issue of February 22.

April 16—Boston University School of Medicine to Conduct a Clinical Meeting at Boston City Hospital.

April 16-20—The American College of Physicians will hold its Eighteenth Annual Clinical Session in Chicago at the Palmer House. For information write Mr. E. R. Loveland, Executive Secretary, 133-135 South 36th Street, Philadelphia, Pa.

April 30—The American Board of Dermatology and Syphilology. Examinations for Certificates. Address: Dr. C. Guy Lane, 416 Marlboro Street, Boston, for details.

July 24-31—The IVth International Congress of Radiology will be held in Zurich under the presidency of Professor H. R. Schniz. General Secretary Dr. H. E. Walther, Gloriastrasse 14, Zurich.

September 3-6—American Public Health Association, at Pasadena, California. Dr. J. D. Dunshee, Chairman, Local Committee on Arrangements.

September 4, 5, 6—International Union Against Tuberculosis will be held in Warsaw. For particulars address The National Tuberculosis Association, 450 Seventh Avenue, New York, N. Y.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH DISTRICT MEDICAL SOCIETY

Wednesday, April 4—Essex Sanatorium, Middleton. Clinic 5 P.M. Dinner 7 P.M. Speakers: Dr. Elliott P. Joslin and Dr. Howard F. Root, Boston. Subject: "Tuberculosis Complicating Diabetes."

Thursday, May 3—Censors' Meeting, at Salem Hospital, 3:30 P.M.

Tuesday, May 8—Annual Meeting. Salem Country Club, Forrest Street, Peabody. Dinner at 7. Speaker to be announced. Subject to be announced.

RALPH E. STONE, M.D., Secretary.
221 Cabot Street, Beverly, Mass.

FRANKLIN DISTRICT MEDICAL SOCIETY

Meetings will be held on the second Tuesday of March and May at the Weldon Hotel, Greenfield, at 11 A.M.

CHARLES MOLINE, M.D., Secretary.
Sunderland, Mass.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

March 14—Meeting notice. See page 561.
Another meeting will take place in May (2nd Wednesday) at Winchester.

ALLAN R. CUNNINGHAM, M.D., Secretary.
76 Church Street, Winchester, Mass.

MIDDLESEX NORTH DISTRICT MEDICAL SOCIETY

Meeting will be held on April 25.

T. A. STAMAS, M.D., Secretary.
226 Central Street, Lowell, Mass.

NORFOLK DISTRICT MEDICAL SOCIETY

March 27—Faulkner Hospital, 8:30 P.M. Dr. Henry H. Faxon and Dr. Edward A. Edwards: Symposium on "Varicose Veins." Discussion by Dr. E. E. O'Neil.

April 17—Hotel Kenmore, 8:30 P.M. Special Business Meeting.

May—Annual Meeting. Time, place and program to be announced.

FRANK S. CRUICKSHANK, M.D., Secretary.
1695 Beacon Street, Brookline, Mass.

NORFOLK SOUTH DISTRICT MEDICAL SOCIETY

April 5—12 noon at Norfolk County Hospital. Speaker: Dr. Elliott P. Joslin. Subject: Diabetes.

May 3—12 noon at Norfolk County Hospital. Annual Meeting. Election of Officers.

N. R. PILLSBURY, M.D., Secretary.
Norfolk County Hospital, South Braintree, Mass.

SUFFOLK DISTRICT MEDICAL SOCIETY

March 28—Clinical Meeting at the Massachusetts Memorial Hospitals.

April 25—Annual Meeting at the Boston Medical Library. Election of Officers. Scientific Program, titles and speakers to be announced.

The Medical Profession is cordially invited to attend these meetings.

JAMES H. MEANS, M.D., Vice-President.
GEORGE P. REYNOLDS, M.D., Secretary,
311 Beacon Street, Boston, Mass.

WORCESTER DISTRICT MEDICAL SOCIETY

All meetings to be held on Wednesdays as follows:

March 14—Dinner and scientific program at the Memorial Hospital, Worcester, Mass.

April 11—Open date.

May 9—Annual Meeting. Time and place to be announced later.

ERWIN C. MILLER, M.D., Secretary.
27 Elm Street, Worcester, Mass.

BOOK REVIEW

Post-Operative Treatment. By GEORGE S. FOSTER, M.D. Published by The Christopher Publishing House, Boston. 323 Pages. Price, $5.00.

This book shows more ignorance of the subject under consideration than any medical book the reviewer has ever had the misfortune to read. It is badly organized, badly written and full of repetitions. Colloquial expressions and trade names of drugs are freely used. The term "Ochsnerization" is used to describe a form of treatment that appears to be diametrically opposed to the ideas shown in Ochsner's original work and to the use of the term in other clinics.

The book has not even the quality of consistency in error. Beginning on page 296 is a chapter entitled "Don'ts." The first paragraph is as follows: "The entire surgical, as well as the entire medical, field is filled with 'don'ts'. Too often cases are overtreated or overdone. Nature plays a most important rôle in bringing back to normal any pathological condition warranting surgical interference, and this assistance must always be considered. Nature is always ready to give." This seems to the reviewer to be excellent doctrine, but all through the book unwarranted, useless treatments are advised at all stages of convalescence. Some of the treatments seem to be to the reviewer positively dangerous, no matter how carefully the technique of the treatment is carried out. For instance, the application of hot wet dressings to the abdomen every four hours following the removal of mildly infected appendices. Other errors are too numerous to mention. There is no index.

It will be unfortunate if the dedication to the graduates of a good medical school is used in any way in an attempt to sell this book to these graduates or to anybody else.